Wednesday 27th April – Afternoon

3 mins presentation.

9 Hidden cardiovascular morbidity in children and young adults born with Congenital diaphragmatic hernia: A Population-based study

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[1]Leeds General Infirmary

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[1]Stanford University School of Medicine, [2]Stanford University, Department of Medicine, Quantitative Science Unit, [3]McGovern Medical School at UTHouston, [4]University of Michigan

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[1]Department of Obstetrics and Gynaecology, Division of Obstetrics and Foetal Medicine, Erasmus MC University Medical Centre, [2]Department of Paediatrics, Division of Neonatology, Erasmus MC University Medical Centre

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Hidden cardiovascular morbidity in children and young adults born with Congenital diaphragmatic hernia: A Population-based study

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Abstract

Introduction

Congenital diaphragmatic (CDH) hernia is a rare congenital malformation with considerable mortality and morbidity in the neonatal period. The majority of the children today survive but little is known about long term cardiovascular morbidity.

Material and methods

This was a nationwide population-based prospective case-control study within a cohort of Swedish children with CDH, born 1982-2015. Five controls for each patient were randomly sampled from the population. The outcomes were the corresponding International Statistical Classification of Disease (ICD) codes for cardiovascular diagnoses according to ICD 9 and 10.

Results

There was an overrepresentation of cardiovascular diagnoses in the CDH group after one year of age compared to the control group, 8.0 %v s 0.5% (n=53 versus n=16). The risk of having a cardiovascular diagnosis in this CDH group was 15 times higher compared to the control group (HR 15.8, 95% CI: 9-27.6, $p < 0.005$). The diagnoses of cardiac arrhythmias and systemic hypertension were less common in the CDH group before the age of one year compared to the CDH group beyond the age of one year. Arrhythmia 3.7 % vs 15.1%, systemic hypertension 3.7 % vs 7.5%.

Conclusion

CDH survivors have increased cardiovascular morbidity during childhood and young adulthood. This implies that structured follow up programs, covering cardiovascular morbidity, needs to be developed and should be offered in pediatric and adult care. Being born with CDH seems to be a risk factor for future cardiovascular diagnoses.

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Pulmonary Function in Scottish children and adolescents with severe congenital diaphragmatic hernia

Mr Paul Burns[1], Dr Jonathan Coutts[1], Dr Emma Box[1], Mrs Colleen Carden[1], Dr Emma Box, Dr David Young[2]
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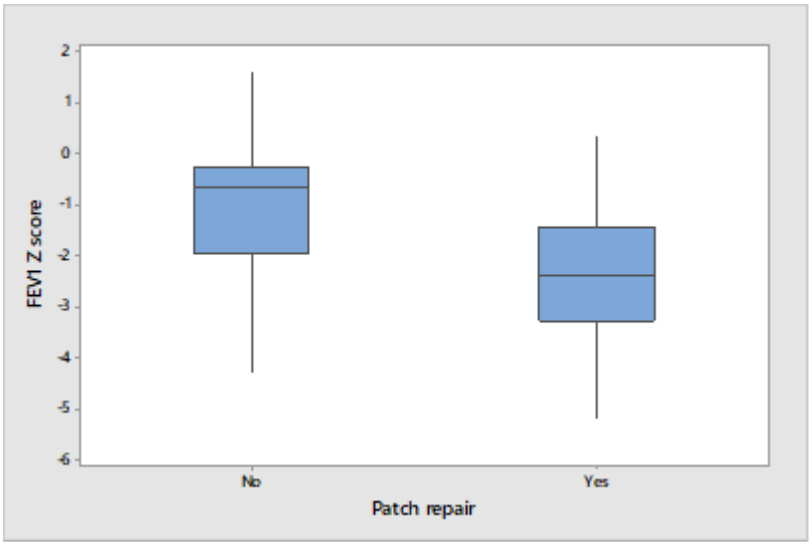
Background:
Survival of infants born with severe congenital diaphragmatic hernia (CDH) is improving. Long term respiratory outcome of affected children is uncertain. Abnormalities in both airway development and lung growth have been described. We review the pulmonary function test (PFT) data from children attending our CDH clinic and compare those with severe CDH requiring a patch repair to those treated without.

Methods
Children are currently followed up in our long term CDH clinic with lung function testing performed routinely. We compared children who underwent PFTs between 2013-2022 with and without severe CDH. We chose FEV1 Z score as the best comparator lung function measurement as this value will be reduced when either airway development or lung growth is abnormal.

Results
55 patients with a mean age of 11.4 years had spirometry performed with 45 also performing static lung volumes. 42% of results were normal. 35% showed an obstructive pattern, 4% restrictive and 20% mixed. The mean FEV1 Z scores were significantly lower when a patch repair was required (-2.40 vs -1.07 p = 0.001). See figure 1.
Of the 22 who had a direct bronchial challenge test, only 3 did not show bronchial hyperreactivity. Whereas only 5 out of 30 patients showed significant reversibility in their baseline FEV1 to a short acting bronchodilator.

Conclusion
Patients who have had repaired CDH have increased lung function impairment. The predominant abnormality is obstructive lung disease. A patch repair is significantly associated with a lower FEV1 Z score compared to those that had a primary repair. A high proportion of patients have a positive bronchial challenge test. Patients with CDH should have long-term follow up including lung function testing once old enough to assess potential impairment.

Images


2
1
0
-1
-2
-3
-4
-5
-6
FEV1 Z score
No
Yes
Patch repair

123

Perinatal factors associated with mortality in Congenital Diaphragmatic Hernia: The Yorkshire Experience

Dr Amy Young[1], Dr Hannah Shore, Dr Amy Young
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Background
Wide inter-unit variability in outcomes in CDH is reported, suggesting significant differences in management exist.
This study aimed to identify perinatal factors associated with mortality in our own high volume centre.

Methods
Cases of confirmed CDH between April 2015 – August 2020 were reviewed.

Results
45 cases were identified. Birth weight ranged from 1.5 – 4kg, Gestation 30+0 – 41+1.

All of the 76% of babies diagnosed antenatally were in-born. None received mask ventilation at delivery. In the first 2 hours of life, 56% had a mean Pmax, 45% a pH and 36% a pCO2 in the target range.
75% received iNO, 79% underwent echo within 24 hours, 9% were discussed with an ECMO centre, with none receiving ECMO.

For those with an antenatal diagnosis, spontaneous delivery was associated with an increased risk of death (55% vs 20%), as was being born out-of-hours (43% vs 29%).
Mortality was strongly associated with having had an antenatal diagnosis (56% vs 1%), use of higher Pmax during the first 2 hours of life (25cmH2O vs 29cmH2O), higher 1st arterial lactate (2.4 vs 6.17) and prolonged use of iNO.

Conclusions / points for consideration
In agreement with multi-centre data, we demonstrate poorer outcomes associated with lower gestation and presence of an antenatal diagnosis.

We also report an association between mode of delivery and poorer adherence to physiological parameters during the first critical hours of life, with death.

Areas for improvement in our own unit are multiple, but may resonate with others.
Development of a pre-brief, supporting early neonatal care has been undertaken and is being piloted.
Revision of guidance surrounding timing and mode of delivery, should be a priority.
The use of early and repeated echocardiography to rationalise pulmonary vasodilator and inotropic therapy should be considered, as should earlier discussion with ECMO centres.

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Long Term Functional Outcomes in Critically Ill Neonates with Congenital Diaphragmatic Hernia

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INTRODUCTION: Congenital diaphragmatic hernia (CDH) is a critical congenital defect with morbidity. There are limited studies describing long term functional outcomes in CDH survivors. We aimed to examine clinical characteristics and serial change in functional status scale (FSS) after hospital discharge in CDH survivors.
METHODS: Single-center retrospective cohort study of infants with CDH. Baseline demographics and disease-specific variables were collected. We extracted data to calculate FSS scores at 4 timepoints up to 12-months after discharge. We excluded patients that died before discharge. We recorded median composite and domain-related FSS scores up to 1 year after discharge.
RESULTS: Data was reviewed for 220 patients from Jan 2009 to Dec 2019. 45 (20%) patients died before discharge. FSS data was analyzed for 165 newborns (58% male, average birth weight 3.07 kg. CDH was left-sided in 78%. Defect sizes were A (25%), B (30%), C (32%), and D (4%). Median CDH risk score was 2.00 [2.00, 3.00]. Median [IQR] FSS score at hospital discharge was 8.0 [7.0, 9.0] with 43 (26%) of patients having at least moderate impairment (FSS >8). Median [IQR] FSS at 0–6-month (n=160), 6-12-month (n=150), and at >12 months (n=144) follow-up visits were 7.0 [7.0, 8.0], 7.0 [6.0, 8.0], and 6.0 [6.0, 7.0], respectively. 24 patients (14.8%) had at least moderate impairment at >12-month. Median composite FSS scores decreased by 2.0 points from hospital discharge to the >12-month follow-up. Median feeding domain scores improved by 1.0 [1.0, 3.0] whereas the other median scores remained with no impairment.
CONCLUSIONS: We observed unchanged or improving functional status through one year after discharge in this cohort. FSS scores were characterized as mild (FSS < 8) at discharge and one-year. The feeding domain had the highest level of functional impairment. Optimal feeding practices may impact long-term growth and should be further investigated.

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Prenatal predictors of mortality and morbidity in infants with CDH. 2 years experience in
National medical research center of obstetrics, gynaecology and perinatology,
Moscow, Russian Federation

Prenatal Predictors Of Mortality And Morbidity In Infants With Cdh Egor Syrkashev[1], Artem Burov[1], Julia Podurovskaya[1], Alexander Gus[1]
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Object
To improve prognostic accuracy and reproducibility of MRI and US-derived data in outcomes prediction in fetus with CDH.
Materials and methods

Prospective study included 71 fetuses with CDH according to ultrasound. Possibilities of indicators obtained by MRI were studied: lung to liver signal intensity ratio (LLSIR), total lung volume to thorax volume ratio (TLV/ThV), total lung volume to fetal body volume ratio (TLV/FBV), observed to expected lung volume ratio (o/eTLV), percent of liver herniation (LH), liver to thorax volume ratio (LiTR). By US we used o/e lung to head ratio (o/e LHR), cardiac compression index (CCI). Also we consider Diag-Ga (gestational age at diagnosis by US).

Results

88.7%(63) of the defects were left-sided, liver herniation observed in 52.1%(37), hernia sac in 9,9%(7). Overall survival - 49.3%(29).

In deceased newborns median TLV was 19.3(12.9-25.7), TLV/ThV-15,5(12,2-18,8), TLV/FBV-0,014(0,01-0,016), o/eTLV-31,6(20,9-38,5), LH-23(3,9-31,8), LiTR-15,8(2,2-22,9), LLSIR-72,9(57,5-87,1), o/eLHR-42,9(30,2-51), CCI-1,4(1,2-1,5).

In survived newborns average TLV according to MRI was 31(22,4-41,1), TLV/ThV-23.2(18.6-28.1), TLV/FBV-0,017(0,014-0,021), o/eTLV-43,7(35,5-53,8), LH-0(0-11,1), LiTR-0(0-6,5), LLSIR-82,6(64,8-92,7), o/eLHR-52,5(46,7-70,7), CCI-1,28(1,2-1,3).

ROC AUC for o/eTLV=0.748, TLV/FBV AUC=0.725, TLV/ThV AUC=0.789, LLSIR AUC=0,642, LH AUC=0.767, LiTR AUC=0.766, Diag GA AUC=0.725, o/eLHR AUC=0.642, CCI AUC=0.738.

For proposed method (multivariate data analysis) considering o/eTLV, LH, CCI and Diag-GA ROC AUC was 0.904.

Most significant correlations with postnatal data were found between o/e TLV and days in invasive ventilation (r=-0,587), transition to enteral feeding (days) (r=-0,654) and total bed days (r=-0,626, p<0,001).

Conclusion

Data obtained allow to use our method as a reliable method for predicting outcomes in fetus with CDH.

Graph

	Group 1 newborns: + (n=36)			Group 2 newborns: - (n=35)			P (1n/ 2n)
	Group 1a: Liver up (n=11)	Group 1b: Liver down (n=25)	overall (1n) (n=36)	Group 2a: Liver up (n=26)	Group 2b: Liver down (n=9)	overall (2n) (n=35)	
Gestational age, MRI, week	31,5(25-34)	33,2(32,4-36,1)	33(30-35,9)	32(27,5-34)	32,4(28,8-33)	32(27,5-34)	0,178
Gestational age, US, week	28,7(22,2-33,4)	33,2(32-45,7)	32,7(27,9-34,4)	29,6(24,1-33,4)	28,8(24,2-32,4)	28,8(24,2-33)	<0,05
TLV, ml	22,3(13,4-41,2)	33,4(28,3-41)	31(22,4-41,1)	18,1(12,2-21,9)	25,2(21-26,7)	19,3(12,9-25,7)	<0,001
o/e TLV, Osada,%	70,1(51,5-83,1)	78,1(65,6-98,5)	73,1(60,9-98)	41,8(36,1-58,4)	66,3(52,4-75,8)	57,5(37,8-65,5)	<0,001
o/e TLV, Rypens,%	40,4(34,1-56,6)	44,6(37,5-52,2)	43,4(37,1-55,5)	27,8(20,2-34,7)	38,4(36,3-50,7)	31,6(21,4-40)	<0,001
o/e TLV, Meyers,%	41,4(33,9-54,4)	46,9(36-49,4)	43,7(35,5-53,8)	28,2(20,3-37,9)	37,2(35,2-52,7)	31,6(20,9-38,5)	<0,001
TLV/FBV	0,019(0,013-0,021)	0,017(0,015-0,021)	0,017(0,014-0,021)	0,013(0,009-0,015)	0,014(0,014-0,021)	0,014(0,01-0,016)	0,001
TLV/ThV, %	21,8(16,6-24,7)	23,2(19,7-28,4)	23,2(18,6-28,1)	15,1(11,3-18,6)	16,6(15,4-21,7)	15,5(12,2-18,8)	<0,001
o/e LLSIR,%	81(62,2-85,9)	82,8(66,4-94,3)	82,6(64,8-92,7)	73,1(58,5-78,5)	67,1(50,1-87,8)	72,9(57,5-87,1)	<0,05
*LH, %	17,5(7,1-22,5)	-	0(0-11,1)	28,8(20,7-32,2)	-	23(3,9-31,8)	<0,001
*LiTR, %	13,2(7-21,1)	-	0(0-6,5)	20,1(14,4-24,7)	-	15,8(2,2-22,9)	<0,001
o/e LHR,%	53(46-72,9)	52(47-67)	52,5(46,7-70,7)	38,7(30-51)	50(47-50)	42,9(30,2-51)	0,001
CCI	1,3(1,2-1,34)	1,26(1,16-1,3)	1,28(1,2-1,3)	1,4(1,29-1,5)	1,3(1,2-1,37)	1,4(1,2-1,5)	<0,001

* data is presented as median (interquartile range), p – Mann–Whitney test

Images

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MEDIASTINAL SHIFT ANGLE IN CONGENITAL DIAPHRAGMATIC HERNIA: PERINATAL AND SHORT-TERM OUTCOMES

MD Laura Valfre[1], MD Andrea Conforti[1], MD Anita Romiti[1], MD Milena Viggiano[1], MD Isabella Fabietti[1], MD Annabella Braguglia[1], Dr Lucilla Ravà[1], MD Marta Luisa Ciofi degli Atti[1], MD Leonardo Caforio[1], Prof Pietro Bagolan[1,2]

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Aim: Mediastinal shift angle (MSA) is a new prenatal predictor of severity and mortality in congenital diaphragmatic hernia (CDH) patients. Aim of our study was to evaluate possible predictive role of MSA on perinatal and short-term outcomes of CDH infants.

Methods: Retrospective cohort study was performed on isolated left CDH patients between 2014 to 2020. MSA was detected between 26° and 29° week of gestation. Perinatal outcomes considered: Feto, gestational age, birth weight, ECMO, stomach and liver up, diaphragmatic defect (A/B vs C/D), need of patch repair, length of ventilation, NICU stay, pulmonary hypertension, oxygen therapy and mortality. Short-term outcomes at 3, 6 and 12 months: neurocognitive alterations, hearing loss, late pulmonary hypertension, respiratory function exams, thoracic anomalies, artificial nutrition, weight and stature gain, late mortality. We used the Receiver Operating Characteristic (ROC) curve methods to define cut-off points and areas under curves (AUC)

Results: 38 patients were included. MSA predict mortality at discharge (p=0.025), dimension of diaphragmatic defect (p=0.010) and need of patch repair (p=0.006). MSA also correlate with thoracic anomalies at 12 months (p=0.023). The cut-off MSA for mortality at discharge is 41.53° (sensitivity 54.55%, specificity 92,59%). The cut-off MSA of thoracic anomalies at 12 months is 39.47° (sensitivity 62.50%, specificity 88,89%).

Conclusions: MSA is a simple and reproducible prenatal predictor of mortality, defect size and need of patch repair. Our data suggest the utility of MSA during routine 2nd trimester US; future prospective studies are needed to confirm our preliminary findings on early and late outcomes

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Image-based prenatal predictors correlate with postnatal survival, extracorporeal life support use, and defect size in left congenital diaphragmatic hernia

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Background: Neonatal outcome prediction in congenital diaphragmatic hernia (CDH) using prenatal imaging has impact on counseling and delivery planning. This study's objective is to evaluate the association between prenatal imaging predictors of patients with left-sided CDH (LCDH) and postnatal outcomes.

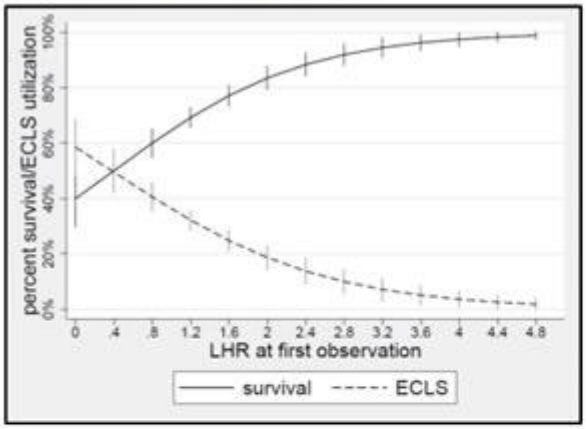
Methods: CDH study group (CDHSG) data were reviewed for LCDH infants born January 2015-October 2019. Prenatal ultrasound and magnetic resonance imaging (MRI) data were collected and correlated with postnatal information including CDHSG defect size [A through D or non-repair (NR)], liver position, ECLS utilization, and survival.

Results: 929 LCDH patients from 85 centers within 17 countries were included. Both prenatal US (LHR and o/e LHR) and MRI (o/e TLV and PPLV) correlated with postnatal survival (72.2%) and ECLS use (29.6%). Logistic regression models confirmed increased survival and decreased ECLS use with larger values for all predictors (Figure). Ultrasound showed decreasing values of LHR and o/e LHR associated with larger defect sizes ($p<0.001$ for both) and post hoc-testing demonstrated that o/e LHR was more closely associated with defect size ($p<0.001$). Prenatal MRI showed similar trends using both o/e TLV ($p<0.001$) and PPLV ($p<0.001$). Importantly, all prenatal values evaluated showed no significant difference between defect size D and NR patients (LHR $p=1$, o/e LHR $p=1$, o/e TLV $p=0.687$, and PPLV $p=0.972$).

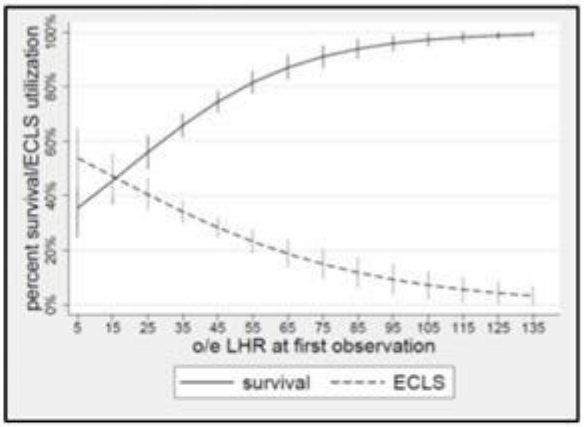
Conclusions: This is the largest cohort of LCDH patients with pre and post-natal data and demonstrates that prenatal imaging factors correlate with postnatal outcomes. The analysis confirms that patients in the non-repair (NR) group are prenatally similar to type D defects and are appropriately classified as severe.

Images

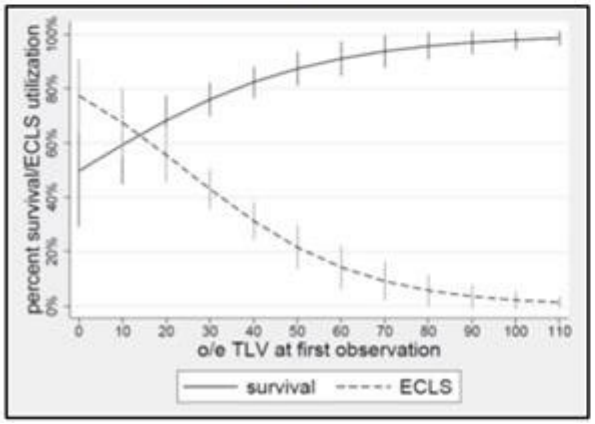
A. Lung to Head Ratio



B. o/e Lung to Head Ratio



C. o/e Total Lung Volume



D. Percent Predicted Lung Volume

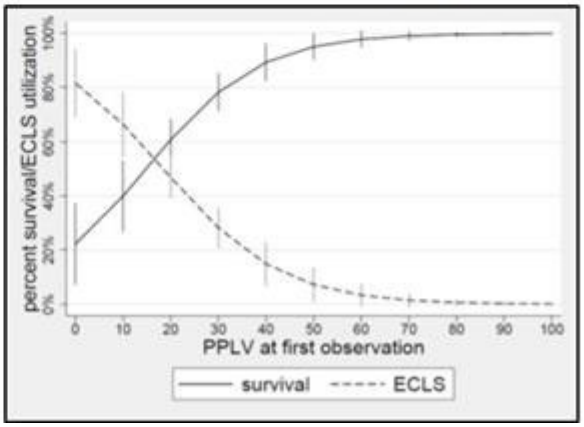


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Image-based prenatal predictors of survival, extracorporeal life support, and defect size in right-sided congenital diaphragmatic hernia

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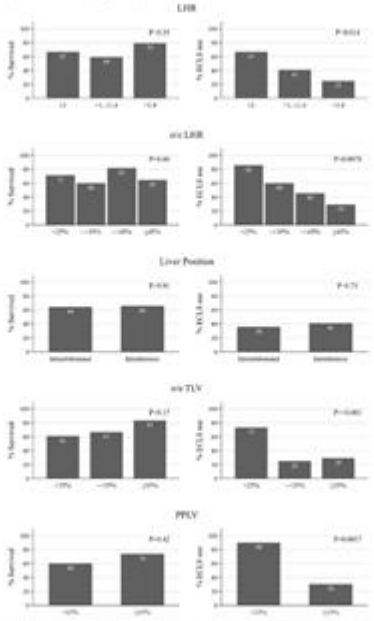
Background
To determine the association between prenatal ultrasound (US) and magnetic resonance imaging (MRI) characteristics in right congenital diaphragmatic hernia (RCDH) with postnatal outcome.
Methods
CDH Study Group data were reviewed for all RCDH infants (n=156) born between 2015 and 2019. Prenatal ultrasound information including lung-to-head ratio (LHR) and observed-to-expected (o/e) LHR as well as fetal MRI evaluation including o/e total lung volume (TLV) and percent predicted lung volume (PPLV) were collected when performed between 18 to 38 weeks' gestation. Liver position was determined by ultrasound and/or MRI. Defect size was determined at the time of operation. The primary outcomes were survival, ECLS use, and defect size. Association between image-derived predictors and outcomes were made using ANOVA for continuous variables and Chi-square test for categorical variables. Logistic regression analysis was used to identity predictors of outcome and Area Under the Curves (AUCs) were computed.
Results
Overall survival was 64.1% and 40.4% required ECLS. Excluding RCDH neonates that were not repaired (n=32), survival was 80.6%. There was no association between prenatal US or MRI lung size measurements and survival in RCDH ($P>0.05$, for all, Figure 1). The greatest need for ECLS occurred in patients with the most severe image-based lung size measurement categories ($P<0.05$, for all). Lower o/e TLV ($P<0.001$) and PPLV ($P=0.006$) were associated with larger defect size while LHR and o/e LHR were not associated with defect size. Intrathoracic liver herniation was not predictive of survival ($P=0.91$), ECLS use ($P=0.71$), or defect size ($P=0.28$).
Conclusion
Image-based prenatal predictors of survival, ECLS, and defect size are of limited value in RCDH. Only MRI-based lung size measures are associated with defect size in right-sided defects. Extrapolation of prenatal survival and morbidity indicators from left to right-sided CDH is not appropriate. There is an urgent need to develop RCDH prenatal prediction models.

Images

Figure 1: Relationship of Lung Imaging Measures with Survival and ECLS use [a]



(a) P values are from the comparison of survival and ECLS use across categories (Chi-square test).

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Prenatal repeated measurements of pulmonary vascular function in foetuses with left-sided congenital diaphragmatic hernia and moderate to mild pulmonary hypoplasia

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Background: Studies in left-sided congenital diaphragmatic hernia (L-CDH) foetuses with severe pulmonary hypoplasia showed that ultrasound parameters for pulmonary function differ compared to healthy controls. In severe L-CDH these parameters also have predictive value for neonatal respiratory morbidity, which could be valuable in prenatal counselling. We aimed to compare these pulmonary vascular parameters between moderate or mild L-CDH foetuses and healthy controls, and to evaluate the predictive value of the parameters for need for treatment of pulmonary hypertension (PH).

Methods: Repeated measurements of the right lung or right pulmonary artery were performed in foetuses with isolated L-CDH (2012-2018) and healthy controls. Ultrasound scans were performed between 18-24 weeks (US1), 24-30 weeks (US2) and 30-33 weeks (US3) gestational age. We assessed the vascularization index (VI), pulsatility index (PI) and peak end diastolic reversed flow (PEDRF). We compared these parameters between L-CDH and healthy controls, and analysed the correlation between these parameters and need for treatment of PH amongst L-CDH foetuses.

Results: Fifty-one L-CDH foetuses and 71 healthy controls were included. At US1, data of 35 L-CDH foetuses was available and 97% (n=34) showed either moderate (n=15, 43%) or mild (n=19, 54%) pulmonary hypoplasia based on the observed-to-expected lung-to-head ratio and liver position. Survival in L-CDH neonates was 78% (n=40) and 51% (n=26) required PH treatment. In L-CDH foetuses preliminary data show significantly reduced VI (US1, US2, and US3: $p<0.02$), increased PI at US2 and US3 ($p<0.05$), and increased PEDRF values at US1 and US3 ($p<0.02$) compared to healthy controls. Analysis in L-CDH for the prediction of need for treatment of PH is ongoing.

Conclusions: In foetuses with moderate to mild L-CDH, preliminary data show significant aberrant VI, PI and PEDRF values compared to healthy controls. Analysis of the predictive value of these parameters for need for treatment of PH is ongoing.

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LUNG RESPONSE AFTER FETOSCOPIC ENDOLUMINAL TRACHEAL OCCLUSION IN RIGHT-SIDED AND LEFT-SIDED CONGENITAL DIAPHRAGMATIC HERNIA

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Background:
Fetoscopic Endoluminal Tracheal Occlusion (FETO) improves survival in selected fetuses with congenital diaphragmatic hernia (CDH). However, it is still unclear which factors affected percentage of lung response after FETO (%LR) and whether %LR is correlated with survival at discharge.

Method:
This is a retrospective study in CDH fetuses undergoing FETO between 2002 and 2021 at UZ Leuven. Cases were included if they had at least two observed-to-expected-lung-to-head-ratio (o/eLHR) measurements after FETO in the clinical reports. Recorded measurements were done a weekly basis (week1-week4). Included variables were: hernia side, o/e LHR at FETO, gestational age (GA) at FETO, percentage of o/e difference (%LR), and survival at discharge. Univariate analysis and/or multiple regression were conducted to investigate the effect of variable and %LR.

Results:
A total of 166 fetuses met the inclusion criteria. Table 1 displays the %LR on a weekly basis. A univariate analysis showed that %LR at week2 was significantly affected by the hernia side (p=0.036), o/eLHR at FETO, and GA at FETO (r2 = 0.13, p=0.009; r2=0.17, p=0.001, respectively). Furthermore, for left(L)-CDH, only GA at FETO had an effect on %LR at week2 (p=0.006). For right (R)-CDH, only LHR at FETO had an effect on %LR at week2 (p=0.0003). In addition, LHR at FETO and GA at FETO also had significant effect on %LR at week 3 (r2 = 0.06, p=0.026; r2=0.11, p=0.003, respectively). There were no correlations between survival and %LR at any of the time points.

Conclusions:
The percentage of lung response at 2 weeks and 3 weeks after FETO are affected by o/e LHR at FETO and GA at FETO. In addition, the hernia side only had a significant effect on %LR at 2 weeks after FETO. The %LR does not predict survival at any time point.

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Ex utero intrapartum therapy in infants with congenital diaphragmatic hernia

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Objective： Previous studies have shown that ex utero intrapartum therapy (EXIT) is safe and feasible for newborns with congenital diaphragmatic hernia (CDH), but the effect of EXIT on the survival rate of children with CDH has not been clarified. This study reports our experience with EXIT in fetuses with CDH, in an attempt to assess whether EXIT can improve the survival of this population.

Design： A retrospective analysis of the clinical data of 116 children with CDH was conducted. The children were assigned into EXIT and non-EXIT groups. Propensity score matching (PSM) towards clinical data was performed and the clinical characteristics and outcomes were compared. Taking survival at discharge as the main outcome, logistic regression analysis was carried out to identify the effect of EXIT on survival.

Results： Thirty of 116 children received EXIT. After PSM, the survival rates of the EXIT group and non-EXIT groups were 82.76% and 48.28% (P=0.006). EXIT [OR=0.083 (0.013–0.525), P=0.008], liver herniation [OR=16.955 (2.342–122.767), P=0.005], and gestational age at diagnosis [OR=0.662 (0.497–0.881), P=0.005] were independent prognostic factors affecting survival of children with CDH. Ninety-nine of 116 children underwent surgery. Liver herniation [10.451 (1.641–66.544), P=0.013] and gestational age at diagnosis [OR=0.736 (0.577–0.938), P=0.013] were independent prognostic factors affecting survival of children after surgery.

Conclusions： EXIT is safe and feasible and can effectively increase survival rate of infants with CDH.

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Left ventricular rotational mechanics in CDH

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Background
Early cardiac dysfunction, affecting both right (RV) and left ventricle (LV) is increasingly recognized as a key component of CDH pathophysiology.
Normal LV function is characterized by systolic, circumferential and longitudinal shortening as well as apical and basal rotation generating twist. LV twist contributes to 60% of left ventricular ejection. LV twist in CDH may be an important determinant of cardiac function and dysfunction.

Methods
Retrospective single center cohort analysis of CDH cases between 2017 and 2021. Ventricular function data was obtained from 1st ECHO at <24 hrs of age. Speckle tracking analysis was used to derive left ventricular systolic global strain in longitudinal (GLS), circumferential (GCS), and radial (GRS) planes, and circumferential rotation at the base and apex Twist was calculated as the difference in rotation between apex and base. Comparison was made with published normative control data.

Results
Complete data was obtained on 38 infants. GLS, GCS, GRS and basal rotation were significantly reduced in CDH compared to controls consistent with previous studies, Table 1.
Basal rotation was significantly reduced in CDH (0.41 ± 6.970 vs. -2.0 ± 1.40, p<0.001)

There was no significant overall difference in LV twist in CDH compared to controls (5.5 ± 9.20 vs. 4.1 ±2.20, p=0.39). In 14 (37%) of cases supra-normal twist values were observed. In 15 (39%) cases reduced twist was observed, Fig 1.

Conclusion:
- Measurement of left ventricular rotational dynamics is feasible in CDH.
- Early postnatal abnormalities in ventricular strain CDH are accompanied by reduced LV basal rotation.
- Increased apical rotation and twist may be a compensatory mechanism in the failing LV.

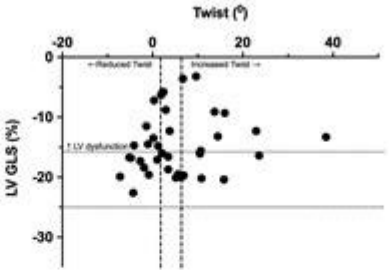
Images

Table 1. LV strain and rotational mechanics in CDH

LV indices	CDH mean (SD)	Published Controls mean (SD)	P value
LV GLS (%)	-15.0 (5.6)	-21.2 (4.9)	**<0.001**
LV GCS (%)	-11.4 (6.8)	-15.6 (4.2)	**<0.001**
LV GRS (%)	16.2 (14.6)	40.7 (26.8)	**<0.001**
LV Apical rot (°)	4.9 (5.2)	4.3 (1.5)	0.47
LV Basal rot (°)	0.4 (7.0)	-2.0 (1.4)	**0.04**
LV Twist (°)	5.5 (9.2)	4.1 (2.2)	0.37

LV, left ventricle; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain.

Figure 1: LV longitudinal strain and LV twist in CDH cases



LV GLS: Left ventricular global longitudinal strain.
Lines represent normal range (mean + SD).

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Cardiac ventricular wall thickness in fetuses with congenital diaphragmatic hernia (CDH)

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[1]Medical and Surgical Department of the Foetus - Newborn - Infant Bambino Gesù Children's Hospital, [2]Neonatal Intensive Care Unit Royal Hospital for Children

Background: Hypoplasia of the developing heart in CDH is an established finding although little is known about the myocardial structure itself. The objective of this study was to assess ventricular wall thickness in fetuses with CDH and the relationship with outcomes.

Methods: Retrospective study, including 12 fetuses with CDH and 12 gestation-matched controls. Right ventricular wall thickness (RVWT), left ventricular wall thickness (LVWT) and interventricular septum thickness (IVSWT) were serially assessed at 24–26, 30–32, and 35–37 weeks of gestational age (GA).

Results: In CDH cases, no significant differences were found between LVWT, RVWT and IVSWT at 24–26 weeks' GA. LVWT and IVSWT were significantly thicker in CDH compared to controls at 30-32 and 35-37 weeks gestation. A similar trend was found for RVWT in the same groups (Table 1). No significant association was observed between ventricular width and main outcomes including survival, ECMO use, duration of intubation or hospital stay.

Conclusions:
Ventrical wall thickness is globally increased in fetuses with CDH later in gestation.
These findings may suggest adaptative cardiac remodeling as a possible response to fetal cardiac compression, or a primary structural alteration. Of note, comparable myocardial hyperplasia in observed in fetuses with Hypoplastic Left Heart Syndrome.
Further investigation of myocardial developmental biology and function in CDH is indicated

Images

Table 1: Ventricular wall thickness in CDH fetuses and controls at three gestational time periods

	CDH (n=12)	Controls (n=12)	p value
Group 1: *GA 24-26 weeks*			
LV thickness, mm (range)	2.7 (1.8-4.7)	2.6 (2.2-3.3)	0.5
RV thickness, mm (range)	3.1 (2.2-6.1)	2.6 (2.2-3.2)	0.2
IVS thickness, mm (range)	2.9 (2.1-4.9)	2.9 (2.2-3.8)	0.8
Group 2: *GA 30-32 weeks*			
LV thickness, mm (range)	3.9 (3-5.3)	3.1 (2.4-3.7)	**0.01**
RV thickness, mm (range)	4 (2.6-4.2)	3 (2.5-4)	0.05
IVS thickness, mm (range)	4.3 (3.1-5.6)	3.1 (2.2-3.6)	**0.0006**
Group 3*: GA 35-37 weeks*			
LV thickness, mm (range)	4.7 (3.5-5.7)	3.7 (2.7-5.2)	**0.01**
RV thickness, mm (range)	5.1 (2.3-7)	3.8 (2.6-6.1)	0.05
IVS thickness, mm (range)	5.2 (2.9-6.8)	3.9 (2.7-6)	**0.04**

Right ventricular (RV), left ventricular (LV), Interventricular septum (IVS), Gestational age (GA)

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Fetal cardiac dimensions in congenital diaphragmatic hernia: relationship with gestational age and postnatal outcomes

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Objective: To serially assess fetal cardiac dimensions in congenital diaphragmatic hernia (CDH) and their relation to disease severity.
Study design: Retrospective analysis of CDH cases and matched controls. Mitral (MVd) and tricuspid (TVd) valve diameters, left (LV) and right (RV) ventricular length and area, Z-scores, were serially assessed at 24-26, 30-32, and 35-37 weeks gestational age (GA).
Results: In CDH cases MVd, MVd Z-score, and LV area were significantly reduced at 24-26 and 35-37 weeks GA. TVd, TVd Z-score, and RV area were significantly reduced at 24-26 weeks. RV area Z-score increased with advancing GA. MVd and MVd Z-score were significantly lower at 24-26 weeks GA in CDH who had a combined outcome of death and/or ECMO.
Conclusions: LV hypoplasia in CDH is characterized by reduced MVd from 24 weeks GA. MVd, and the ratio of mitral and tricuspid valve diameters at later gestations, may be potential predictors of disease severity.

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Prophylactic administration of prostaglandin E1 is associated with a reduced risk of death in the first year of life in neonates with moderate to severe left congenital diaphragmatic hernia (CDH)

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Introduction:
In neonates with CDH, associated with pulmonary hypertension can be predictive of higher morbidity and mortality rates. Pulmonary vasodilator treatments don't improve survival.
To assess the effects of prophylactic administration of prostaglandin E1 (PGE1) in neonates with moderate to severe left CDH. We performed a retrospective review between 2010 and 2018. Moderate CDH was defined as o/e LHR between 26 to 35% liver "down" or between 36 to 45% liver “up”, the severe group was defined based on o/e LHR between 15 to 25%.
We compared the morbidity and mortality of infants in this cohort according to whether or not they received prophylactic treatment with PGE1.

Results:
139 infants with CDH were care at Lille Hospital during this period. 39 infants with antenatal diagnosis of isolated left sided moderate or severe form of CDH. 13 infants received prophylactic PGE1. They were compared to 26 neonates who did not receive the prophylactic treatment. The two groups were similar in terms gestational age (39.7±1.4GW vs 39.1±3.1GW, p=0.4) and birth weight (2983±600g vs 3121±750g, p=0.4). The prophylactic group had worse o/e LHR (36±9 vs 47±14, p=0.02).
The mortality rate at 12 months of age was null in the group of infants who received the prophylactic treatment of PGE1, whereas it was of 6 out of 26 in the second group of neonates who did not receive the prophylactic treatment (p=0.02).

Conclusion:
Prophylactic use of PGE1 in infants with moderate to severe left CDH is associated with a reduced risk of death in the first year of life. As one of the PGE1 physiological effect on neonates is to maintain ductal patency, we hypothesize that patent ductus arteriosus may support cardiorespiratory function early in life in infants with moderate to severe CDH.

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THE UTILITY OF SERIAL ECHO PARAMETERS IN THE MANAGEMENT OF NEWBORNS WITH CONGENITAL DIAPHRAGMATIC HERNIA(CDH)

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Introduction: Around 40% of newborns with CDH maybe born with either left or right ventricular or biventricular dysfunction due to ventricular interdependence and secondary to persistent pulmonary hypertension. Association of ventricular dysfunction and ventricular performance is not only a predictor for disease severity, but also mortality and need for ECMO.
Methods: Retrospective review of data from CDH-Qatar (CDH-Q) registry. Timed echocardiography (ECHO) performed at four intervals -a) within 72 hours of birth, b) 24-48 hours pre-operative, c) 24-48 hours post-operative, d) fourth week of life or before discharge, if earlier.
Results: 42 newborns with CDH were admitted during study period (M/F:19/23), with median gestation of 38 weeks (IQR:36-39) and birth weight 2.83 kg (IQR 2.45-3.17). Twenty-nine were left-sided, 7 right-sided, 1 central, and 3 bilateral diaphragmatic hernias. Eight had associated congenital heart disease and genetic abnormalities in 33%. Total 12 (30%) died in early infancy of which (5 -genetic anomalies, 3 preterm, and one growth restricted) and 2 required ECMO. ROC analysis of preoperative Respiratory severity score (RSS) revealed AUC was 0.9410, with a sensitivity of 92.3 7% and a specificity of 89.7% predicting mortality at a cut-off value of 4.9. A total of 119 echos in 40 newborns (2 excluded, 1 palliated since birth and other with severe anomalies) were analysed, where available at the agreed time intervals. Markers of elevated pulmonary pressures (RVSP, bidirectional shunting, TPV/RVET ratio) and subnormal TAPSE were useful in guiding therapy, use of milrinone and sildenafil, but no correlation could be made with outcome data. Fifty-eight percent (7/12) of newborns who died had moderate to severe PH in first 72 hours.
Conclusion: Serial timed functional ECHO monitoring allows targeted therapy of patients with CDH. Preoperative RSS and the initial severity of pulmonary hypertension may be useful in predicting mortality.

Images

Table 1: Predictors of Mortality

1A. Comparison of Demographic and clinical characteristics of infants with CDH based on outcome of mortality			
	No Mortality	**Mortality**	***p-value***
Number of patients	28	12	
*Gestational age (weeks),	38(37-39)	37 (34-38)	NS
*Birth weight (grams)	2.95(2.73-3.44)	2.45(1.7-3.4)	NS
Gender (male%)	12(42%)	6(50%)	NS
Genetic Anomalies (N %)	5(17.8%)	5[a](42%)	NS
*Age at surgery (days of life); Median (IQR)	5(3-15)	8 (3-10)	NS
*Pre-operative MAP (mmHg)	12(11-15)	11.5 (10-15)	NS
*Pre-operative FiO_2 (%)	32(25-58)	53(35-80)	NS
*Post-operative MAP (mmHg)	14 (12-21)	18(10-26)	NS
*Post-operative FiO_2 (%)	62(46-88)	65(48-100)	NS
Pre-operative inotropic use (#VIS) (Median)	7.5(7-8)	16	NS
Post-operative inotropic use (#VIS) (Median)	12.5(8-17)	13	NS
Milrinone treatment Post-op	6(21%)	4(33%)	NS

1B. Comparison of ECHO parameters of infants with CDH based on outcome of mortality			
Pre-operative (Pre-op) Pulmonary Pressure i)RVSP[$], ii) PDA (Bidirectional/Right to left shunting) iii) PAAT/RVET ratio <0.3 (N%) iv) Septal flattening	 35(20-45) 4(14.2%) 5(17.8%) 9(32%)	 44 (32-66) 3/6(50%) 3/6(50%) 3/6(50%)	 NS
Preop TAPSE (mm), Median	8	8	NS
Post-operative (Pre-op) Pulmonary Pressure i)RVSP ii) PDA (Bidirectional/Right to left shunting) iii) PAAT/RVET ratio <0.3 iv) Septal flattening	 25(20-60) 6(21%) 5(18%) 5(18%)	 60(45-90) 2/6(33%) 2/6 (33%) 2/6(33%)	 NS
Post-op TAPSE (Median)	8	9	NS

[a]Genetic Anomalies -Trisomy 13, Mosaic trisomy of 1q, Congenital myasthenia gravis, Phelan-McDermid syndrome, Chromosome 12p duplication (Pallister-Killian syndrome) and Wolf-Hirschhorn syndrome (WHS)
MAP- Mean Airway pressure; (Respiratory severity score (RSS)= MAP X FiO2)
RVSP- Right Ventricular Systolic Pressure
PDA-Patent Ductus Arteriosus
PAAT- Peak Acceleration Time
RVET- Right ventricular ejection time
TAPSE- Tricuspid annular plane systolic excursion
* Median [25th Centiles, 75th Centiles]; [$]Median(Range)
# Vasoactive Ionotropic score(VIS): (dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + 100 × epinephrine dose (μg/kg/min) + 10 × milrinone dose (μg/kg/min) + 10 000 × vasopressin dose (unit/kg/min) + 100 × norepinephrine dose (μg/kg/min).

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Brain natriuretic peptide levels in children with congenital diaphragmatic hernia-related pulmonary hypertension treated with treprostinil

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Purpose: Pulmonary hypertension (PH) accounts for significant morbidity and mortality in congenital diaphragmatic hernia (CDH), especially when refractory to standard treatment. Treprostinil, a synthetic prostacyclin-analog and potent pulmonary vasodilator, is increasingly used to treat patients with PH related to developmental lung diseases but indicators of efficacy are lacking. We aimed to describe the association between treprostinil and brain natriuretic peptide (BNP), a biomarker representing PH and right ventricular dysfunction, in children with CDH-related PH treated with treprostinil.

Methods: We conducted a retrospective review of prospectively collected data from all patients with CDH treated with treprostinil at our quaternary care center between April 2013 and September 2021. Treprostinil was administered to patients with severe PH with a component of right ventricular dysfunction, refractory to inhaled nitric oxide. Treprostinil was titrated to an initial dose of 20 ng/kg/min over 48 hours and then increased based on clinical and echocardiographic effect. BNP levels were measured at least once per week based on clinical status. Data were obtained from medical records and are reported as percentage or median (range). The distributions of BNP values were compared to the baseline values using the Wilcoxon signed rank-tests (RStudio), adopting p=0.05 as level of significance.

Results: Fifty-one patients were treated with treprostinil for a median of 67 days (2-427). Most patients had left-sided defects (84%) and thoracic liver herniation (84%). All but six patients required extra-corporeal membrane oxygenation (88%) and most defects were repaired using a Gore-Tex patch (82%). Following treprostinil initiation, BNP levels (pg/mL) decreased at one week [314.4 (38.8-2552.5), p=0.149], two weeks [208.9 (17.1-2346.0), p=0.006] and one month [120.5 (11.1-2490.6), p=0.004] (Figure). Despite decreasing BNP levels, mortality in this cohort remained high at 39% (20/51).

Conclusion: Upon starting treprostinil treatment, BNP levels decrease over time in children with severe CDH-related PH.

Images

Evolution of BNP after start of Treprostinil administration