Thursday 28th April 13.30 – 13.55
Live Abstract Presentations in MAIN AUDITORIUM, live streamed with recording

34 The predictive scoring system of small diaphragmatic defect in infants with congenital diaphragmatic hernia.

Dr. Keita Terui[1], Dr. Kouji Nagata[2], Dr. Masaya Yamoto[3], Dr. Masahiro Hayakawa[4], Prof. Hiroomi Okuyama[5], Dr. Shoichiro Amari[6], Dr. Akiko Yokoi[7], Dr. Taizo Furukawa[8], Prof. Kouji Masumoto[9], Dr. Tadaharu Okazaki[10], Dr. Noboru Inamura[11], Dr. Katsuaki Toyoshima[12], Dr. Yuki Koike[13], Dr. Manabu Okawada[14], Dr. Yasunori Sato[15], Dr. Noriaki Usui[16]
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58 Impact of bowel rotation and fixation on obstructive complications in congenital diaphragmatic hernia

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40 Neonatal rodent ventilation and clinical correlation in congenital diaphragmatic hernia – defining "gentle" ventilation

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93 METABOLIC AND LIPIDOMIC PROFILING OF THE EFFECTS OF TRACHEAL OCCLUSION IN A RABBIT MODEL OF CONGENITAL DIAPHRAGMATIC HERNIA

Dr TRH Regnault[1], Dr Martina Mudri[3], Dr S Zhao[4], Dr Shane A Smith[3], AZ Buzatto[4], J Li[4], R Duruisseau-Kuntz[4], J Davidson[5], L Li[4], Dr Andreana Butter[5]

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The predictive scoring system of small diaphragmatic defect in infants with congenital diaphragmatic hernia.

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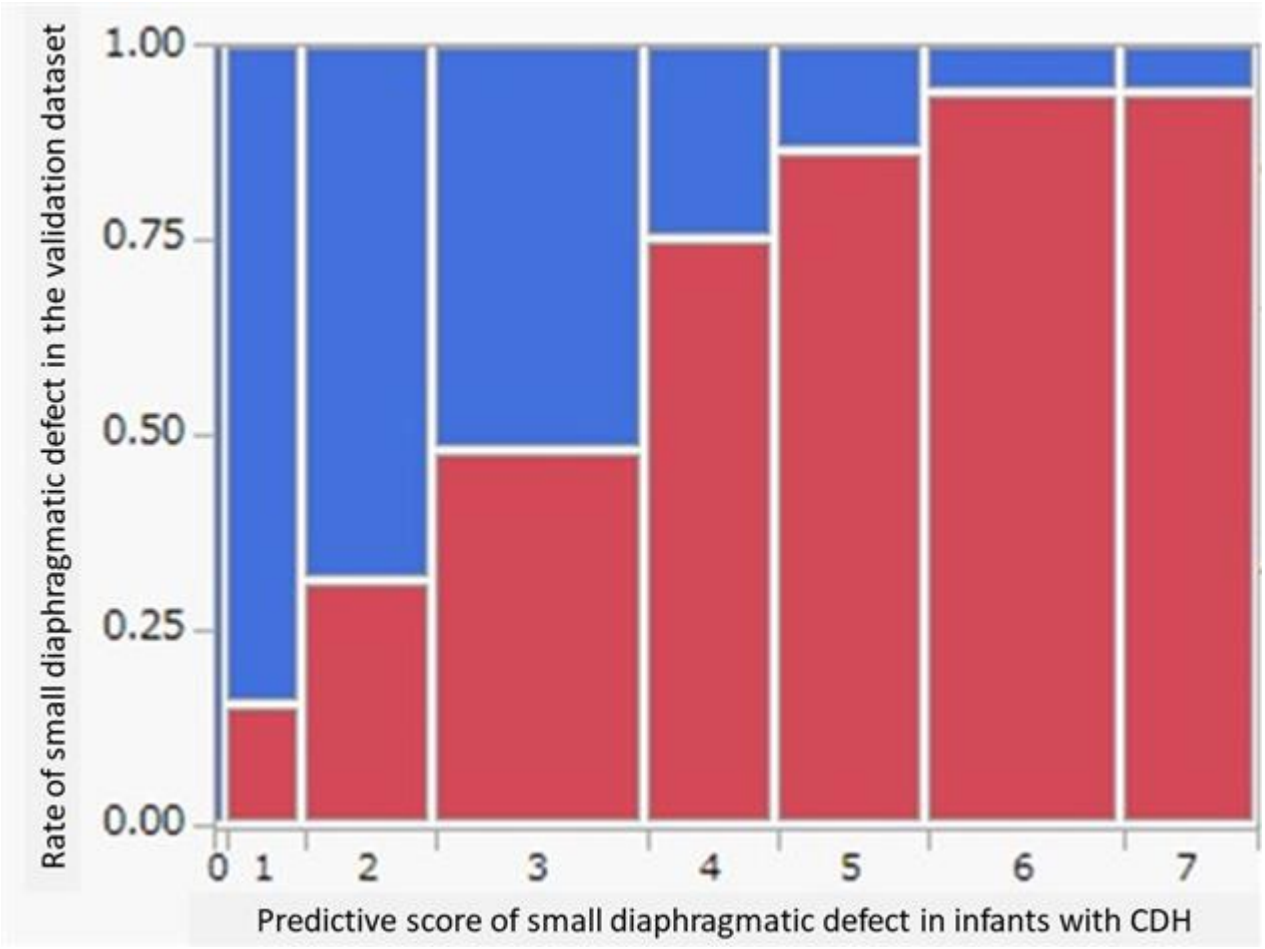
Background: A size of diaphragmatic defect is crucially important factor in thoracoscopic surgery for congenital diaphragmatic hernia (CDH). We aimed to establish and validate a predictive score of small diaphragmatic defect in infants with CDH.

Methods: In a Japanese CDH study group database among 2006 and 2020, patients with left isolated CDH who underwent surgery for CDH were included in this study. Cohort was randomly divided into derivation (n = 397) and validation (n = 396) datasets. Using a logistic regression analysis, we created a prediction model and weighted scoring system of small diaphragmatic defect (international classification; A and B) from the derivation dataset. Variables were selected by forward-backward stepwise selection method with Akaike's Information Criterion. The obtained model was validated using the validation dataset.

Results: The selected six variables were weighted proportionally to their adjusted parameter estimates for small diaphragmatic defect: No hydramnios, 1 point; Apgar score (1 min) of 5 - 10, 1 point; apex type of the lung (the left lung is detected in the apex area radiographically), 1 point; oxygenation index <8, 1 point; abdominal nasogastric tube (tip of nasogastric tube is detected in abdominal area radiographically), 2 points; no right-to-left flow of ductus arteriosus, 1 point. Rates of small diaphragmatic defect for the possible- (0-3 points), probable- (4-5 points), and definite- (6-7 points) groups were 36%, 81%, and 94%, respectively ($p < 0.001$), in the validation datasets. Sensitivity, specificity, positive predictive value and the C statistics in the validation datasets were 0.78, 0.79, 0.88 and 0.76 for probable group, and 0.45, 0.94, 0.94 and 0.70 for definite group, respectively.

Conclusion: Our simple scoring system effectively predicted the small diaphragmatic defect in infants with CDH, which is useful to determine whether thoracoscopic surgery is indicated.

Graph


Rate of small diaphragmatic defect in the validation dataset
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
Predictive score of small diaphragmatic defect in infants with CDH

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Small Bowel Obstruction after neonatal repair of Congenital Diaphragmatic Hernia – results from a large longitudinal cohort-study

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Background:
In patients with congenital diaphragmatic hernia (CDH) postoperative small bowel obstruction (SBO) is a life-threatening event. An incidence of 20% and an association with patch repair and ECMO-treatment have been reported. This longitudinal cohort study aimed at identifying the incidence of SBO and risk factors of surgical, pre- and postoperative treatment.
Methods:
We evaluated all consecutive CDH survivors born between January 2009 and December 2017 using a standardized prospective long-term follow-up program.
Results:
337 patients were included, with a median follow-up of four years. SBO with various underlying causes was observed in 38 patients (11.3%) and significantly more often after open surgery. The majority of SBO required surgical intervention (92%). Adhesive SBO (ASBO) was detected as the leading cause in 17 of 28 patients, in whom surgical reports were available. Duration of chest tube insertion (OR 1.22; 95% CI 1.01–1.46, p=0.04) was identified as an independent predictor for ASBO in multivariate analysis. Beyond the cut-off value of 16 days, the incidence of serous effusion and chylothorax was higher in ASBO-patients (ASBO/nonSBO: 2/10 vs. 3/139 serous effusion, p=0.04; 2/10 vs. 13/139 chylothorax, p=0.27). Type of diaphragmatic reconstruction, abdominal wall closure or ECMO-treatment showed no significant association with ASBO. A protective effect of one or more reoperations has been detected (RR 0.16; 95% CI 0.02–1.17; p=0.049).
Conclusions:
Thoracoscopic CDH-repair significantly lowers the risk of SBO. Neonates produce more proinflammatory cytokines and have a reduced anti-inflammatory capacity, which may contribute to the higher incidence of ASBO in patients with longer duration of chest tube insertion, serous effusion and chylothorax– as well as to the protective effect of reoperations. In future, novel therapeutic strategies based on a better understanding of the pathophysiology of adhesion formation might contribute to a reduction of peritoneal adhesions and their associated morbidity and mortality.

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Impact of bowel rotation and fixation on obstructive complications in congenital diaphragmatic hernia

Kamila Moskowitzova[1], Jill Zaliecka[1], Catherine Sheils[2], Ronald Becker[3], Mollie Studley[1], Lindsay Lemire[1], David Zurakowski[1], Terry Buchmiller[1], Dr. Terry Buchmiller

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Background

Small bowel obstruction (SBO) is a known complication after congenital diaphragmatic hernia (CDH) repair. Some patients undergo surgical intervention and may even require extensive bowel resection, resulting in short bowel syndrome (SBS). We investigate whether specific rotation and fixation of the bowel can be used as a predictor for obstructive complications including midgut volvulus.

Methods

A single center retrospective review was performed of 256 surviving patients following CDH repair from 2003 to 2020. Operative notes and upper gastrointestinal series (UGI) were screened to determine the rotation and fixation of the bowel. We defined malrotation as abnormal position of ligament of Treitz and nonfixation as lack of lateral colonic attachments. Primary outcomes included occurrence of SB0, SBO treated surgically, and midgut volvulus. For statistical analysis Fisher's exact test was utilized and significance was defined as $P<0.05$.

Results

Twenty-two (9%) patients presented with SBO and most of these, 19 (86%), required surgery. SBO was caused by adhesions in 11 patients (58%), recurrence in 5 (26%), and midgut volvulus leading to SBS in 3 (16%). Median age at complication was 1 year (0.1-10 years). Rotation and fixation status were both recorded in 117 (46%) patients (Table). Presence of left (L) CDH with malrotation and nonfixation was a significant predictor for SBO and SBO requiring surgery ($P<0.05$ vs all other groups). All 3 patients with volvulus had L CDH with nonfixed bowel (100%), however only 1 had malrotation (33%).

Conclusions

Malrotation and nonfixation are associated with increased obstructive complications in CDH. Normal rotation is not protective and patients are still at risk for volvulus resulting in SBS. SBO requiring surgical intervention is common in CDH. Bowel rotation and fixation are important determinants that, should be routinely documented and education about the risk of SBO should be included in family counseling.

Images

Table Bowel status and obstructive complications

Bowel rotation and fixation n=117	Small Bowel Obstruction		Small Bowel Obstruction Requiring Surgical Intervention				
		P		P	Adhesions	Recurrence	Volvulus with SBS
Left CDH no malrotation / fixed	0/1 (0%)	0.999	0/1 (0%)	0.999	0/1 (0%)	0/1 (0%)	0/1 (0%)
Left CDH no malrotation / nonfixed	5/53 (9.4%)	0.193	4/53 (7.6%)	0.254	2/53 (4%)	0/53 (0%)	2/53 (4%)
Left CDH malrotation / nonfixed	10/39 (25.6%)	0.025 *	9/39 (23.1%)	0.014 *	6/39 (15.4%)	1/39 (2.6%)	1/39 (3%)
Right CDH no malrotation / fixed	1/2 (50%)	0.271	1/2 (50%)	0.226	1/2 (50%)	0/2 (0%)	0/2 (0%)
Right CDH no malrotation / nonfixed	0/7 (0%)	0.591	0/7 (0%)	0.596	0/7 (0%)	0/7 (0%)	0/7 (0%)
RIght CDH malrotation / nonfixed	1/15 (6.7%)	0.694	0/15 (0%)	0.21	0/15 (0%)	0/15 (0%)	0/15 (0%)

* P<0.05 vs. all other groups

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Neonatal rodent ventilation and clinical correlation in congenital diaphragmatic hernia – defining “gentle” ventilation

Dr. Vikas Gupta[1], Dr. Cory Wilson[1], Ms. Elizabeth Popp[1], Dr. Siqin Zhaorigetu[1], Dr. Scott Collum[1], Ms. Di Jin[1], Dr. Amir Khan[1], Dr. Harry Karmouty-Quintana[1], Dr. Matthew Harting[1]
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Introduction:
Ventilator management is a critical part of managing congenital diaphragmatic hernia (CDH). We aimed to use a murine model and patient data to study CDH-associated differences in oxygenation, airway resistance, and pulmonary mechanics by disease severity.

Methods:
We used the nitrofen model of CDH. For control and CDH rodents, data were collected within the first hour of life. Oxygen saturations (SpO2) were collected using MouseOx, and large airway resistance and inspiratory capacities were collected using FlexiVent. A single-center, retrospective review of term CDH infants from 2014-2020 was performed. Tidal volumes were collected every 6 hours for the first 48 hours of life or until the patient was taken off conventional ventilation. Newborns that were mechanically ventilated but had no pulmonary pathology were used as controls. CDH severity was defined using CDH Study Group (CDHSG) classification system.

Results:
Control rodents had a median SpO2 of 94.4% (IQR 87.6–97.5%), and CDH pups had a median SpO2 of 27.9% (IQR 22.4-30.4%)(p<0.01)(Fig.1A). There was no difference in large airway resistance between CDH and control rodents(Fig.1B). CDH rodents had lower inspiratory capacity than controls (median 267□L,IQR 216–352 vs. median 110□L,IQR 70-170;p<0.01) (Fig.1C). Thirty CDH and ten control infants were included. Fourteen patients were CDHSG Stage A/B, thirteen CDHSG Stage C/D, and three patients were unrepaired. CDH infants had a lower initial SpO2 and lower tidal volumes than controls (median 4.2mL/kg, IQR 3.3 – 5.0 vs. 5.4mL/kg, IQR 4.7 – 6.2; p=0.03). When risk-stratified, there was no difference in tidal volume between controls and low-risk CDH patients. High-risk CDH infants had significantly lower tidal volumes than controls.

Conclusion:
CDH infants have lower SpO2 and tidal volumes than infants without pulmonary pathology. The nitrofen CDH model reflects these differences. Rodent ventilation models may be useful in developing tailored ventilatory strategies, based on risk, for CDH infants.

Images

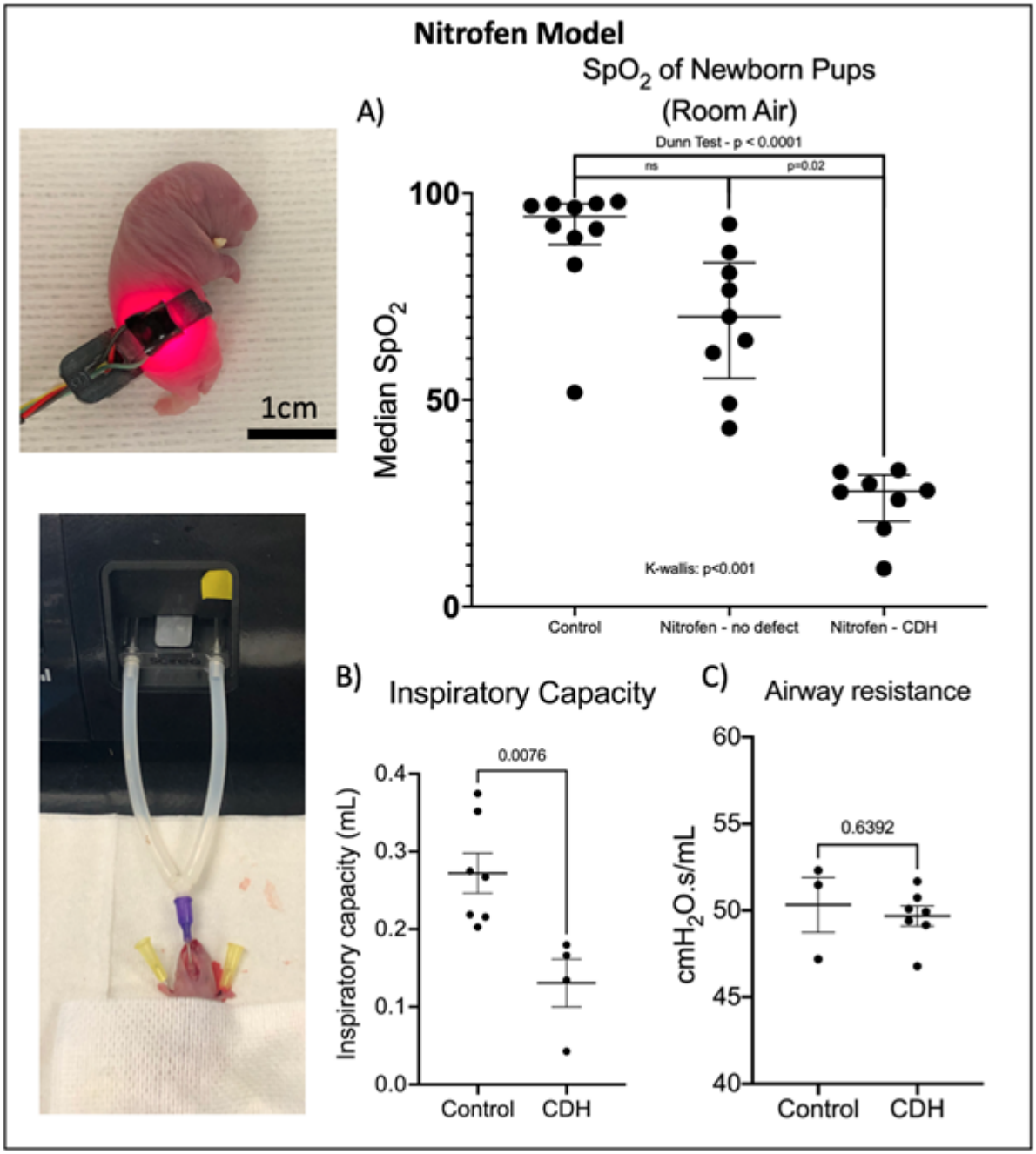

Figure 1

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METABOLIC AND LIPIDOMIC PROFILING OF THE EFFECTS OF TRACHEAL OCCLUSION IN A RABBIT MODEL OF CONGENITAL DIAPHRAGMATIC HERNIA

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PURPOSE: Fetal tracheal occlusion (TO) reverses the pulmonary hypoplasia associated with CDH. 'Omic' readouts capture metabolic and lipid processing function, acting as unique biomarkers to better understand CDH&TO.

METHODS: CDH was created in fetal rabbits at 23 days, TO at 28 days and lung collection at 31 days (Term~32 days). Lung-body weight (LBWR) and mean terminal bronchiole density (MTBD) were determined. Left and right lungs were collected, weighed, and pooled as cohort samples, homogenized and extracts collected. Metabolomic and lipidomic data were collected using chemical isotope labeling LC-MS with Dansyl- and DmPA-labeling and isotope-assisted LC-MS and LC-MS/MS respectively. Volcano plot univariate analysis, principle component analysis and partial least squares discriminant analysis as multivariate analysis tools analyzed the metabolomic and lipidomic data (IsoMSPro1.2.10,NovaMT-Metabolite Databasev2.0,LipidScreener1.0). Pathway analysis was conducted with MetaboAnalyst with HP-CIL metabolomic data.

RESULTS: LBWR was significantly lower in CDH while CDH+TO was similar to controls($p=0.003$). MTBD was significantly higher in CDH fetuses and restored to control levels in CDH+TO($p<0.001$). CDH and CDH+TO resulted in significant differences in liver metabolome and lipidome profiles compared to controls. Volcano plots, for both metabolites and lipids revealed a number of significantly altered metabolites and lipids between the control and CDH groups and the CDH and CDH+TO fetuses (when using FC≥1.50o ≤0.667 and p-value adjusted for false-discovery rate (FDR-p)<0.05 as the criteria for significance). Significant changes in arginine and proline metabolism between control and CDH were observed and in glycine, serine and threonine metabolism between CDH and CDH+TO.

CONCLUSION: CDH+TO reverses pulmonary hypoplasia in the CDH rabbit, in association with a specific metabolic and lipid signature. A synergistic untargeted 'omics' approach provides a global signature for CDH and CDH+TO, highlighting the common cellular mechanisms among lipids and other metabolites, enabling comprehensive network analysis to identify critical metabolic drivers in disease pathology and recovery.