Optimal Management of Congenital Diaphragmatic Hernia: Are we there yet?

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Disclosures

I have no relevant financial relationships with the manufacturer of any commercial product and/or provider of commercial services discussed in this CME activity

Visiting Utah? Top 10 Things you should know...

1. SLC is an Olympic City

2. HQ for the LDS Church
3. Greatest Snow on Earth
4. Great National Parks
5. There are bars and liquor stores
6. Great Salt Lake is really salty
7. 1st State with an official “state firearm”
8. Marijuana is not legal in Utah
Intro
• CDH remains one of the most frustrating major lung birth defects to manage
• Estimated to occur 1 in 2000 to 4000 live births
• Despite advances in care, still associated with a high risk of mortality and morbidity in survivors

CDH
• Impaired pulmonary/vascular development, leads to severe lung hypoplasia and PPHN
  – 90% develop severe respiratory insufficiency
  – 20 to 40% require ECMO

Etiology
• Developmental defect of the diaphragm occurs at 8 to 10 weeks gestation
• Majority isolated (non-syndromic)
• Associated major congenital anomalies occur in 10-40%
  – cardiac in 15-25% (severe 5-10%...TOF, coarctation, TGA, HLHS)
Genetics

- Isolated CDH felt to be a multi-genic disease, arise from de novo mutational events
  - low risk of familial/sibling recurrence 0.9 to 2.0%
- Ongoing studies potential candidate chromosomal regions
  - GATA4, NR2F2
- Syndromic causes include Fryn’s (AR), Pallister-Killian (chrom 12), trisomy 13, 18 and 21, Pentalogy of Cantrell

CDH Anatomic Types

- Bochdalek (posterior lateral)- most common
- Morgagni (anterior)
- Par sternalis (central)
  - 85% left sided
  - 13% right sided
  - 2% bilateral
Prenatal

• 2/3 of cases prenatally diagnosed by 2nd or 3rd trimester

LHR

• Varying Techniques, Timing/GA critical

Liver Herniation

• Liver herniation
  
  No: 79% survival  
  Yes: 41% survival

  • May not just be a matter of “Up vs. Down”…MRI may help refine outcome prediction

Prenatal

• Lung/Head ratio
  
  - <10% if LHR < 1.0, >1.4 80-100%
  
  • Liver in chest, worse prognosis
    
    - Higher rate ECMO (~75%) and lower survival
  
  • Lung MRI: PFLV < 30%, poor prognosis
  
  • Other Predictive Variables:
    
    - Chromosomal anomalies, prematurity, LBW, right-side lesions

LHR Risk Stratification

• Defining Liver “Up”

  • Quantification by MRI better predictor of just “Up vs. Down”
  
  • 21% or greater herniation associated with mortality or need for ECMO (p<.001)
Fetal Surgery

- To date, human trials (EURO Fetus and UCSF) have NOT demonstrated significant benefit vs. controls
- FETO (Fetal Endotracheal Occlusion) trials ongoing
  - TOTAL trial (Tracheal Occlusion To Accelerate Lung Growth)- Deprest Belgium PI
  - Enrolling fetuses with high predicted mortality based on LHR and liver position
  - Balloon 27-30 wks, remove electively at 34 wks

FETO Postnatal Survival?

Difficult to interpret data and compare between centers…

CDH Hidden Mortality

- Typical reported “survival” range 50 to 70% live born infants, 30 to 40% overall
- Often centers report 80 to 90% survival but data usually only represent liveborn
  - Major case selection bias (pregnancy termination, non-resuscitation, death prior to tertiary center, etc.)
  - Population based studies more realistic

Outcomes of Congenital Diaphragmatic Hernia: A Population-Based Study in Western Australia
Joanne Colvin, Carol Bower, Jan E. Dickson and Jami Sokol
Pediatrics 2007;119;356-363
DOI: 10.1542/ped.2004-2148
- Western Australia 1991 – 2002
- 116 cases of CDH identified in birth defects registry
  - Included miscarriages, stillbirths and abortions
  - 53% prenatal diagnosis, 49% terminated
- 71 (61%) born alive
- 37 survived beyond 1 year
  (52% of liveborn, 32% overall)

Colvin, Peds 2005

- CHOP (1996-2000)
- Review of 174 CDH prenatal diagnosis with and without CHD/Other anomalies
  - Liveborn, survival 58%
  - Overall survival 43%
    - 24 termination, 9 fetal demise

Cohen et al, J Peds 2002; 141:25

- 18% with CHD, 29% with additional significant non-cardiac anomalies

Liveborn: 8000+ CDH cases

Mortality based on defect (<1% to 50%)

Staging based on defect size, +/- CHD

Lally, Sem Perinatol 2014

Lally, Sem Perinatol 2014
Long Term Outcome

- Still lots of non-survivors despite improvements in care over time…
- Morbidity multifactorial, highest in patch repair and ECMO survivors
  - Chronic lung disease, pulmonary hypertension, reactive airways, GER, feeding difficulty, hearing and neurocognitive impairment

So...Can we improve Outcomes?

Best Approach?

- No single-center with enough volume to conduct a large randomized trial
- Difficult to organize multi-center study…personal and individual center dogma makes collaboration difficult
- Majority of recommendations, therefore, come from database review, observational studies, individual center experience

Levels of Evidence

- Single most important tool to improve outcomes for each center is to have a consistent, consensus-driven standardized protocol (evidenced based as much as possible)
Individual Center Reports

- Preliminary observations of the use of high-frequency jet ventilation as rescue therapy in infants with congenital diaphragmatic hernia. *J Peds Surg* 2010;45:698-702

Key Consensus Points in CDH Care…

I. Optimize Prenatal Care and Outborn Referral

- Delivery at a tertiary center with experience in neonatology, pediatric surgery, cardiology and ECMO improves outcomes
  - Families should be given option
- Optimal delivery around 38 weeks EGA
- Avoid Preterm Delivery

Prenatal Referral

II. Regionalized Care, Experience

• Responsible escalation of care
  – Should not wait until fail maximum support, i.e., HFV, multiple vasopressors, iNO, etc.
• Location and distance key consideration
  – Good communication with regional referral center vital
  – Up to 15-20% die during or waiting for transport

Timely Transport if Outborn...

Center Case Volume

• Likely an important factor...
• Encourage regionalization of care

Survival: HVC vs LVC

Grushka, J Ped Surg 2009
III. Optimizing Postnatal Care

Delivery

- Intubation with avoidance of BMV
- Gastric decompression (NG or OG)
- Avoidance of high airway pressure during resuscitation
  - Limit PIPs < 25-28 cm H₂O
- Gradual increase of pre-ductal oxygen saturations to between 80 and 95%

Oxygenation Goals

- **Initial 1st hour:** accept pre-ductal saturations of > 70%
  - Optimize lung inflation at 9-10 ribs
  - Allow SAT’s to slowly increase w/out overly aggressive ventilator manipulation
- **Between 1-2 hours:** accept pre-ductal saturations of 75% to 85%
- **By 2-3 hours:** Pre-ductal saturations should be > 90-95%
Mechanical Ventilation

- "Gentle ventilation" strategy critical to success
- All "Benchmark Centers" utilize this approach
- Initial 2-3 hours: accept PCO2 of < 65-70 and pH > 7.20

Conventional

- Volume targeted strategy preferred (we use Drager® VN500™)
- SIMV/Volume Guarantee mode, limit set TV 4-5 ml/kg breath and PEEP 4-5 cm
- Avoid PIPs > 25-30 cm H2O
- Unable to limit pressures and keep pH and pCO2 in range...convert to HFV

HFV

- HFOV – Begin with P_{aw} 11-13 cm H2O, Hz 8-10, Amp 24-28
  - In general should NOT increase P_{aw} > 16 cm H2O (If need to increase, confirm with CXR)
- HFJV – Same P_{aw} : I-time at 0.02 sec, Rate 360, PEEP 6-7 cm H2O, PIP 24-28
  - no background rate initially

Which Ventilator?

- Most experience with Sensormedics® HFOV, but also Bunnell® HFJV and VDR-PulseFlow™ HPFV
- All work, principles generally the same
- Recent interest in HFJV as rescue or primary ventilator for CDH
Theoretical Advantages HFJV

- Lower MAP to achieve similar blood gases vs. HFOV
  - improves systemic and pulmonary venous return
- Longer expiratory phase respiratory cycle breaths (IT .02s) vs. HFOV (IT .33s),
  - lessens resistance to cardiac filling and outflow, limits lung over-inflation/air trapping

HFPV- VDR

- Combined Conventional with High Frequency
  - Uses high percussive rates (500-900 bpm) and small tidal volume breaths
  - Convective mode, use Pressure Limited, Time-Cycled breaths and a set rate of 10-30 bpm

Timing of Repair

- Delay Surgery
  - Avoid immediate surgery
  - Fix when “hemodynamically stable”, at least 48-72 hrs
- Reasonable settings:
  - FIO2 < .50
  - PIP ≤ 26-28 cm H2O (conv)
  - PAW < 16 and dP < 30 (HFV)
  - PA pressures ≤ 2/3 systemic
  - Minimal Vasopressor support

IV. Thoughtful Utilization of ECMO

BENEFIT VS. risk?
CDH Criteria for ECMO

- Inability to maintain preductal sats >85%
- Severe resp acidosis
- Ventilator support too high
- Systemic hypotension/worsening metabolic acidosis
- Significant airleak

Not Going to Get Better?

- Reasonable to define lethal lung hypoplasia:
  - NEVER achieving a PCO₂ < 75 or preductal oxygen saturation > 85%
- Not everyone should go on ECMO
  - ~10% of overall case population

VV vs. VA?

When to Repair Once on ECMO?

- On/Off ECMO?
  - Our goal at PCH is to repair off ECMO
  - Consider repair case by case, usually for babies unable to wean off by 14 days
- Other Centers - Mixed Bag
  - Early (0-3 days)
  - Intermediate (3-7 days)
  - Late (7-14 days)

Lally, J Peds Surg 2009
Final Thoughts

- Optimize Prenatal Care/Outborn Referral
- Regionalization
- Protocolized Care
- Gentle Ventilation
- Use ECMO appropriately
  - Long-Term Follow-Up

Why it Matters?

Questions?
Learning Objectives

At the end of this presentation the participant will be able to:

1. Discuss the etiology and prevalence of CDH
2. Understand role of ECMO in management
3. List resuscitation principles of a baby with CDH at delivery
4. Define best practice approach based on consensus guidelines