Surgical Frontiers in NICU Care

Tom Jaksic MD PhD

Surgical Frontiers in NICU Care: the Abdomen

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Disclosures: None

NECROTIZING ENTEROCOLITIS

- Most common gastrointestinal surgical emergency in the neonate
- INITIAL KUB

NEXT DAY

Necrotizing Enterocolitis

Necrotizing Enterocolitis

November 1, 2014
NECROTIZING ENTEROCOLITIS

- Incidence: not well defined
- Reported Mortality: variable (6-63%)
- Pathogenesis: unclear, associated with prematurity/low birth weight
- Diagnosis: lack of uniform criteria
- Treatment: controversial; surgical indications are perforation or clinical deterioration on maximal medical management

Lord Kelvin

“If you can not measure it, you can not improve it.”

Major Problem: single centers see relatively few cases of NEC

Vermont Oxford Network (VON)

> 650 Member Hospitals

Vermont Oxford Network

- Platform for prospective cohort studies
- Data are collected using uniform definitions in Manual of Operations
- Verified and analyzed at VON central office. Data returned for correction as needed.
- Surgery-VON collaboration since 2005

HIERARCHY OF STUDIES

- RCT
- COHORT
- CASE-CONTROL
- CROSS-SECTIONAL
Necrotizing Enterocolitis

Overall Goal
Surgery-VON:

Provide benchmark incidence and mortality data to foster quality improvement and facilitate valid comparisons between centers

Recent Surgery-VON Investigations

1. Incidence and Mortality of NEC expressed by birth weight categories
2. Mortality of Surgical NEC and its relationship to treatment
3. Mortality of Surgical SIP
4. Relationship between congenital heart disease and NEC in VLBW neonates

Methods: VON Database Manual of Operations

- Survival: successful discharge from hospital, or alive in hospital at one year of age (followed if transferred from VON hospital to outside hospital)
- Surgical treatment codes placed in Manual
- NEC diagnosis standardized: laparotomy, post-mortem, specific clinical/radiologic criteria

Methods: Definition of NEC

- Clinical and Radiologic Criteria
  - Clinical findings (≥1):
    - Bilious gastric aspirate
    - Emesis
    - Abdominal distention
    - Occult/gross fecal blood (no anal fissures)
  - Radiologic findings (≥1):
    - Pneumatosis intestinalis
    - Portal venous gas
    - Pneumoperitoneum

AND

RESULTS

Data Collection;
> 80% of VLBW neonates born in the United States during time interval of studies

The Mortality of Necrotizing Enterocolitis Expressed By Birth Weight Categories


(Journal of Pediatric Surgery 2009;44:1072-5; discussion 5-6)
Results: Incidence of NEC
(n=71,808)

<table>
<thead>
<tr>
<th>Birthweight (g)</th>
<th>Category 1 (501-750g)</th>
<th>Category 2 (751-1000g)</th>
<th>Category 3 (1001-1250g)</th>
<th>Category 4 (1251-1500g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of NEC (%)</td>
<td>12%</td>
<td>9.2%</td>
<td>5.7%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

P < 0.001

Results: Mortality
(n=66,849)

<table>
<thead>
<tr>
<th>Birthweight (g)</th>
<th>Category 1 (501-750g)</th>
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<th>Category 3 (1001-1250g)</th>
<th>Category 4 (1251-1500g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>42%</td>
<td>29.4%</td>
<td>21.3%</td>
<td>15.9%</td>
</tr>
</tbody>
</table>

P < 0.001

Results: Odds Ratio of Mortality

<table>
<thead>
<tr>
<th>Birthweight (g)</th>
<th>Category 1 (501-750g)</th>
<th>Category 2 (751-1000g)</th>
<th>Category 3 (1001-1250g)</th>
<th>Category 4 (1251-1500g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>No NEC (n=66,849)</td>
<td>NEC (n=4,958)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR 1.6</td>
<td>OR 3.6</td>
<td>OR 7.5</td>
<td>OR 9.9</td>
</tr>
</tbody>
</table>

P < 0.001

Summary

- Benchmark data are available
- Birth weight is crucial to understanding
  - NEC incidence
  - NEC mortality
  - Odds ratio for mortality

Clinical Progression Predictors?

- None that are clinically useful


Surgical NEC Treatment Controversy

- Laparotomy vs. primary peritoneal drainage

- COCHRANE REVIEW: “Evidence from two RCTs suggests no significant benefits or harms of peritoneal drainage over laparotomy. However, due to the very small sample size clinically significant differences may have been easily missed. No firm recommendations can be made for clinicians.”
The Mortality and Management of Surgical Necrotizing Enterocolitis in Very Low Birth Weight Neonates: a Prospective Cohort Study

Hull MA, Fisher JG, Gutierrez IM, Jones BA, Kang KH, Kenny M, Zurakowski D, Modi BP, Horbar JD, Jaksic T

J Am Coll of Surg 2014;218:1148-1155

Specific Aims

- Prospectively collect data on VLBW neonates to quantify the mortality of Surgical NEC in the United States
- Assess the utilization and associated mortality of laparotomy and PPD

Incidence Data Summary

- 9% of VLBW neonates diagnosed with NEC
- 52% of NEC neonates had surgical NEC
- 69% of surgical NEC neonates had a laparotomy rather than PPD (P < 0.001)
- 46% of the PPD group also had laparotomy

Percentage of NEC Managed Surgically

* P < 0.05
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Number of NEC Patients by Birth Weight Category

<table>
<thead>
<tr>
<th>Birth Weight (Grams)</th>
<th>Medical NEC n = 8,221</th>
<th>Surgical NEC n = 8,935</th>
</tr>
</thead>
<tbody>
<tr>
<td>401-500</td>
<td>211</td>
<td>345</td>
</tr>
<tr>
<td>501-750</td>
<td>2,267</td>
<td>3,608</td>
</tr>
<tr>
<td>751-1000</td>
<td>2,501</td>
<td>2,823</td>
</tr>
<tr>
<td>1001-1250</td>
<td>1,886</td>
<td>1,391</td>
</tr>
<tr>
<td>1251-1500</td>
<td>1,356</td>
<td>768</td>
</tr>
</tbody>
</table>

Surgical Mortality Summary

- Surgical NEC had a significantly higher mortality than Medical NEC overall (35% vs. 21%; P < 0.005) and for each birth weight category > 750 grams (P < 0.0001); mortality plateau of ~30%
- By multivariable logistic regression analysis birth weight, surgical NEC, and PPD were the significant independent predictors of mortality

Mortality by Surgical Intervention

- The mortality of laparotomy vs. PPD with laparotomy was similar (31% vs. 34%, P = 0.42)
- PPD alone (n = 1,521) was associated with a significantly higher mortality (50%, P < 0.0001)
- CAUTION: FROM THESE COHORT DATA CAUSALITY CANNOT BE DETERMINED (Patient selection factors vs. treatment effects are hard to differentiate)

Mortality by Surgical Intervention

- Was PPD applied to a more ill group than laparotomy?
- PPD overall was used more frequently in neonates who had cardiac compressions and endotracheal intubation at birth (P < 0.05, and P < 0.02 respectively)
The Mortality Associated with laparotomy-confirmed Neonatal Spontaneous Intestinal Perforation (SIP); a Prospective 5-year Multicenter Analysis

Fisher JG, Jones BA, Gutierrez IM, Kang KH, Kenny M, Zurakowski D, Modi BP, Horbar JD, Jaksic T

*J of Pediatr Surg 2014;49:1215-1219*

Spontaneous Intestinal Perforation

- First described in 1981
- Initially described as a variant of NEC
- Mortality not well documented

Comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>SIP (%)</th>
<th>Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids for Lung Disease</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Patent Ductus Arteriosus (PDA)</td>
<td>12</td>
<td>39</td>
</tr>
<tr>
<td>Indomethacin Administration</td>
<td>52</td>
<td>26</td>
</tr>
<tr>
<td>PDA ligation</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Indomethacin and Steroids</td>
<td>12</td>
<td>5</td>
</tr>
</tbody>
</table>

All P < 0.001

Mortality Data by Surgical Intervention

- Was there a subset in the PPD treatment arm that did very well?
- 50% of PPD alone group (27% of whole PPD group) survived without receiving a laparotomy; does this reflect a subgroup with minimal NEC (or SIP) that reconstituted their bowel without further surgery?

Mortality of SIP (n=804)

<table>
<thead>
<tr>
<th>Birth Weight (g)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>401-500</td>
<td>n=32</td>
</tr>
<tr>
<td>501-750</td>
<td>n=370</td>
</tr>
<tr>
<td>751-1000</td>
<td>n=243</td>
</tr>
<tr>
<td>1001-1250</td>
<td>n=108</td>
</tr>
<tr>
<td>1251-1500</td>
<td>n=51</td>
</tr>
</tbody>
</table>

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Summary

The overall mortality of laparotomy-confirmed SIP in VLBW neonates is 19%

For neonates >750g, the mortality of SIP is significantly greater than baseline

The mortality of SIP is ~½ that of surgical NEC

Relationship Between Serious Congenital Heart Disease (CHD) and NEC in VLBW Neonates

- Most recent VON/Surgical Collaboration (Presented at 95th New England Surgical Society Annual Meeting September 2014)
- CHD (n=1931) significantly increases the risk of NEC in VLBW infants (13 vs 9%)
- Mortality of CHD and NEC is 55%; significantly higher than either alone
- AV canal and Trisomy 21 are independent risk factors for NEC in VLBW neonates

Overall Summary

- Slightly over half of VLBW neonates with NEC have surgical NEC
- Birth weight based benchmark mortality data for surgical and medical NEC now exist
- The mortality associated with surgical NEC remains extremely high and is significantly greater than medical NEC (accentuated in VLBW neonates > 750 g)
- Surgeons perform laparotomy significantly more frequently than PPD (over 2/3 of cases, P < 0.001)
- the mortality for laparotomy ≠ PPD and laparotomy < PPD alone (P < 0.0001), however, this may just reflect selection bias
- Optimal operative management for NEC remains to be defined (RCTs focused on specific patient subsets may be of utility)
The incidence and mortality of NEC is highly predicted by birth weight:

<table>
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<th>Incidence of NEC (%)</th>
<th>Mortality of NEC (%)</th>
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<tbody>
<tr>
<td>501-750</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>751-1000</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>1001-1250</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>1251-1500</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

The mortality of surgical NEC is 35% and plateaus at 30% even for neonates > 750 grams.

The overall mortality of SIP is 19% (higher than one might anticipate); ~½ the mortality than for surgical NEC for any given birth weight.

MANY STUDIES STILL TO BE DONE!