Introducing a new scoring system of abdominal function for early diagnosis of necrotizing enterocolitis in preterm infants

Master thesis in Medicine

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Introducing a new scoring system of abdominal function for early diagnosis of necrotizing enterocolitis in preterm infants

A retrospective analysis

Master Thesis in Medicine, Evelina Lilja
INTRODUCING A NEW SCORING SYSTEM OF ABDOMINAL FUNCTION FOR EARLY DIAGNOSIS OF NECROTIZING ENTEROCOLITIS IN PRETERM INFANTS

Abstract

Title: Introducing a new scoring system of abdominal function for early diagnosis of necrotizing enterocolitis in preterm infants

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Institution, City, Country: Division of Neonatology, Department of pediatrics, Sahlgrenska University Hospital and Sahlgrenska Academy, Gothenburg, Sweden.

Background: Necrotizing enterocolitis (NEC) is an inflammatory disease of the bowel primarily affecting premature infants. Early stages of NEC have been linked to feeding intolerance and affected abdominal status. High morbidity and mortality indicate the importance of early diagnosis.

Objective: To evaluate the Gothenburg Abdominal Scoring system (GAS) to determine if GAS can be used for early diagnosis of Necrotizing enterocolitis in preterm infants.

Methods: A retrospective study of 83 preterm infants born before gestational week 28+0 and treated at the NICU at the Queen Silvia Children’s Hospital in Gothenburg, Sweden. The NEC group (n=39) was diagnosed according to modified Bell’s staging criteria ≥ 2A, and the controls (n=44) were preterm infants not diagnosed with NEC. GAS score is calculated based on feeding volume, change of feeding volume since previous day, gastric residuals and frequency of stools. Data was recorded from the day of NEC diagnosis and 6 days prior. Average age at NEC diagnosis was 13 days; data from the controls were recorded from day 13 of life and 6 days prior. The GAS system would score each parameter resulting in a score from 0-8 per day where a higher score would imply a tendency towards gastrointestinal distress.

Results: Average stools per day during the studied period were 1.8 ± 0.5 in the NEC group and 3.5 ± 0.4 in the control group. Days to passing of first stool was 4 ± 2.3 days in the NEC group and 2.8 ±1.8 days in the control group. Mean total gastric residual volume in the NEC group was 4.3 ± 1.3 mL and 5.8 ± 0.6 mL in the control group. The NEC group had a higher GAS score in total.
Conclusions: NEC patients born before gestational week 28+0 have significantly delayed passage of meconium and significantly lower stool frequency during the days leading up to NEC diagnosis. An upward trend in the GAS system could be seen in the NEC group during these days. This was significant for the studied group as a whole but the relevance for the individual infant remains unclear.

Keywords: Premature, predictors, NEC, gastric residuals, feed intolerance, stool frequency
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>Abdominal Circumference</td>
</tr>
<tr>
<td>BW</td>
<td>Birth Weight</td>
</tr>
<tr>
<td>DSBUS</td>
<td>Queen Silvia Children’s hospital (Gothenburg, Sweden)</td>
</tr>
<tr>
<td>ELBW</td>
<td>Extremely Low Birth Weight &lt;1000 grams</td>
</tr>
<tr>
<td>EUGR</td>
<td>Extra Uterine Growth Restriction</td>
</tr>
<tr>
<td>FI</td>
<td>Feeding Intolerance</td>
</tr>
<tr>
<td>GA</td>
<td>Gestational Age</td>
</tr>
<tr>
<td>GE</td>
<td>Gastric Emptying</td>
</tr>
<tr>
<td>GR</td>
<td>Gastric Residual (volume of gastric aspirate obtained before a feed)</td>
</tr>
<tr>
<td>GRV</td>
<td>Gastric Residual Volume</td>
</tr>
<tr>
<td>NEC</td>
<td>Necrotizing enterocolitis</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>SGA</td>
<td>Small for Gestational Age</td>
</tr>
<tr>
<td>TPN</td>
<td>Total Parenteral Nutrition (also hyperalimentation)</td>
</tr>
<tr>
<td>VLBW</td>
<td>Very Low Birth Weight &lt;1500 grams</td>
</tr>
</tbody>
</table>
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Introduction

Background

Necrotizing enterocolitis (NEC) is an acute ischemic necrotizing disease of the intestine that above all affects premature infants[1] and is one of the most devastating gastrointestinal emergencies among neonates[2]. NEC is often associated with sepsis and is often complicated with perforation of the bowel and peritonitis[3]. The morbidity and mortality is substantial, around 10-40% [1, 4, 5]. The incidence of NEC is about 0.1% in live births but in very low birth weight (VLBW) infants the incidence is approximately 7%[4]. Since the 1960’s, and the birth of modern neonatal intensive care, the incidence of NEC and its associated mortality and morbidity has not improved[2]. In some centers the incidence has even increased[6] and this can be linked to the ever advancing medical care and the NICU’ ability to care for even smaller premature infants[2]. The prevalence of NEC differs between centers but is about 7-11% among VLBW infants[2, 5]. NEC often presents itself after the start of enteral feeds, usually during the first weeks of life.

Infants born at gestational age 23-28 weeks develop NEC several weeks after enteral feeding has begun, the lower the gestational age the longer time till NEC after birth[2, 4, 5]. Infants born at full term who develop NEC are inclined to have specific risk factors such as congenital heart diseases or hypotension. Main risk factors for NEC are prematurity, low birth weight, enteral formula feeding and an atypical colonization of the intestine by bacteria. Additional risk factors are breathing disorders which requires ventilator support and Patent ductus arteriosus (PDA)[4, 7, 8].
The pathogenesis of NEC is not entirely understood but a multifactorial cause has been proposed. A confluence of genetics, immaturity of the bowels, imbalance of the microvascular tone, a highly immunoreactive intestinal mucosa and the possibility of an abnormal microbial colonization of the gut all seem to be predisposing factors[2]. The immaturity of the bowel is comprised of the immature motility, digestion, absorption, circulatory regulators and immune defense.

Clinical signs of NEC include abdominal distention and tenderness, abdominal wall erythema, feeding intolerance and bloody stools[2, 5]. Non-specific signs of NEC that the patient might exhibit are lethargy, apnea, bradycardia and temperature instability that increases the demand of ventilator and vasopressor support[4]. NEC diagnosis is set by using a staging system created by Bell at al., and it is based on physical examination findings, laboratory findings and radiography where stage 1 depicts a mild form of NEC and stage 3 the most severe[2, 4]. Laboratory findings that would implicate NEC are non-specific and include a decrease in platelet and white blood cell count, anemia, metabolic acidosis, hypo- or hyperglycemia, an imbalance in electrolytes and a rise in C-reactive protein. The radiographic findings most specific to NEC are pneumatosis intestinalis, pneumoperitoneum and portal venous gas along with intramural- and intraluminal gas[2, 4, 5].

When the diagnosis of NEC is suspected, medical intervention is the initial management. Medical intervention includes bowel rest, total parenteral nutrition (TPN) and broad-spectrum antibiotics. There are two types of surgical interventions; primary peritoneal drainage (PPD) and laparotomy with resection of the necrotized bowel. With laparotomy the non-viable bowel is removed and often an enterostomy is created[2, 4, 5].
A concern with Bell et al. staging system is that it cannot exclusively detect NEC and it cannot predict severity of the disease[8]. A more specific staging system along with specific biomarkers for NEC could be beneficial when it comes to early diagnosis[8].

The development of the gastrointestinal tract and its immune system benefits from factors found in human milk (e.g. s-IgA) and might reduce the incidence of NEC. Enteral feeding is important for the development of the GI-tract and if the introduction of enteral feeds is delayed or the use of TPN is prolonged the development might be compromised, leading to intestinal atrophy, increased permeability, inflammation and sepsis. It has been seen that increasing enteral feeds to quickly can lead to NEC [1, 2, 6]. In a Cochrane review from 2011 they found no differences in time to reach full feeds or the incidence of NEC when comparing the use of continuous enteral feedings and bolus feedings[10].

Feeding intolerance (FI) is a common problem among VLBW infants. The most common practice in which to measure FI is gastric residuals (GR). GR volume and coloring are observed before enteral, either bolus or continuous, feeds are resumed. GR and FI are considered an early sign of NEC but there is no agreement on what volume or color of the GR constitutes a predictor of the disease since it is common among VLBW infants to have GRs and all do not have NEC.

Today there is no uniform standard in how GRs are managed. There is no consensus in what is a significant GR volume or the importance of its color or whether to discard or return the GR when aspirated. This practice is routine in most NICUs, as a guide for feeding advancements or thought to be an early indicator for NEC[11]. Studies
have shown that maximum residual as a percentage of the corresponding feed and hemorrhagic residuals might be a predictor of NEC[12, 13].

When large GRV or discolored GRs are aspirated before feeds the common practice today is to withhold further feeds. This results in delay and advancement of feeds which in turn can lead to a prolonged use of TPN and an increased risk of late onset sepsis and extra uterine growth restriction (EUGR) which is a risk factor for neurodevelopmental delays and growth inhibition in VLBW infants.

GRs are in turn an indicator of gastric emptying (GE). GE is slower in preterm infants compared to term infants due to the immature bowel of the preterm infants. Early enteral feeding promotes GE because of it speeds up the maturation of the bowel and its functions. GE also increased when preterm infants were given human milk compared to formula. Multiple factors can affect GE; for example drug administration, feed management, PDA, sepsis and NEC.

A randomized case-control study compared two ways of measuring feeding intolerance in VLBW infants, abdominal circumference (AC) and gastric residual volume (GRV) where the goal was to measure time to full feeds. The AC group achieved this earlier and they also had fewer interrupted days and a shorter time in which TPN was used compared to the GRV group. Mortality and hospital stay was comparable but the impact on NEC could not be evaluated, more studies are needed to confirm this strategy. It is still not clear what constitutes a GRV that is indicative of NEC. A wide range of GRV is now accepted and differs from country and center, this leads to the discontinuation of enteral feeds which might be unnecessary and lead to longer hospitalizations[6, 11, 14].
As NEC is known to have a rapid progression it is important with an early diagnosis. This to avoid or hinder the advancement of the disease preferably through therapeutic intervention so not to resort to surgery and resection of the bowel which can lead to intestinal failure and short bowel syndrome[2, 8, 9].

In infants, a working bowel is characterized by feeding tolerance and a regular stool pattern[15]. Most infants born at term pass their first stool within 48 hours of life. Preterm infants however have a known delay of passing their first stool, especially those small for their gestational age (SGA), probably because of the infants’ immature bowel function. The composition of meconium of preterm infants is different from that of term infants. The composition makes it thicker and in combination with the preterm infants’ immature bowel function it makes it tougher to expel.

A study by Bekkali et al. confirmed that the passage of first stool was delayed in premature infants compared to term infants. They also showed that the passage of meconium was prolonged i.e. the transition from meconium to normal stools. Bekkali et al. showed that delayed passage of first stool was associated with low GA, low BW and morphine therapy. They also found that the duration of meconium passage was further delayed by respiratory support. The type of feeding the infants received was not associated with delayed passage of first stool, however TPN caused delay[16, 17].

It has been indicated that there is a correlation between delayed meconium passage and bowel dysfunction and perforation in VLBW infants. Given this, feeding tolerance could be helped by optimizing early bowel function and evacuation of meconium. In one study the VLBW infants were given routine glycerin enema to
promote early meconium passage. They found that the study group passed first meconium faster than the control group. It was also seen that sepsis was less common in the study group and that the incidence of NEC was lower. The study group reached full enteral feeds faster[18, 19]. A study by Haiden et al. used an osmotic contrast agent to see if it could quicken the passage of meconium, it did not. But it was found to stimulate bowel movements, which in turn shortened time to full enteral feeds. The use of the contrast agent was associated with an increased development of NEC[15]. In another study no conformity between the passage of the meconium and NEC was found[20]. A retrospective study compared stools patterns from infants who developed NEC with infants who did not. The infants who developed NEC was found to have significantly more stools and seedy stools than the control group in this study[21].

The present study was undertaken to determine if the parameters; stool frequency, feeding volume, increase or decrease of feeding volume from day to day and gastric residual volume could give indications of NEC.

**Primary hypotheses**

Gothenburg Abdominal Scoring (GAS) can be used as an early indicator to detect NEC in premature infants that are being cared for at a NICU.

**Table 1. The Gothenburg Abdominal Scoring system (GAS)**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteral feeds</td>
<td>Full feeds</td>
<td>Partly</td>
<td>0</td>
</tr>
<tr>
<td>Gastric residuals, &gt;1 ml/kg/meal</td>
<td>0-2 meals/d</td>
<td>2-4 meals/d</td>
<td>&gt;4 meals/d</td>
</tr>
<tr>
<td>Change of feeds since previous day</td>
<td>Increased</td>
<td>Unchanged</td>
<td>Decreased</td>
</tr>
<tr>
<td>Stool/meconium</td>
<td>&gt;2 times/d</td>
<td>1-2 times/d</td>
<td>None</td>
</tr>
</tbody>
</table>
Specific aim

To retrospectively use GAS to study premature infants diagnosed with NEC at the NICU at the Queen Silvia Children’s hospital (DSBUS) in Gothenburg during an 11-year period between the years 2004-2014, to determine if GAS can be used as an early indicator of NEC.

Significance of the study

NEC is a feared condition in premature infants with high morbidity and mortality. To reduce the morbidity and mortality of NEC, early identification and diagnosis is of importance. The use of a valid system to detect early onset NEC by monitoring patterns in the infants’ intestinal function is hereby introduced. GAS could contribute to an earlier identification of the disease and thereby reduce the morbidity associated with NEC.

Material and methods

During the studied period (2004-2014) 97 infants developed NEC at the NICU at Queen Silvia Children’s hospital in Gothenburg. Complete medical records were obtained from 39 infants born before gestational age 28+0 weeks who developed NEC. The control group consisted of 44 infants born between the years 2013-2014 and cared for at the NICU at DSBUS, not diagnosed with NEC. All infants included in the study were born before gestational week 28+0. Medical records from these patients were reviewed in the aspects of GAS (see table 1) to see if GAS could be used as an early indicator of NEC. Data was collected from medical charts that had been scanned in to the medical records system Melior. Data concerning feeding volume (mL) per day via intermittent enteral bolus feeding or continuous enteral
feeding was collected. Gastric residuals; total volume per day, largest GRV per day and amount of GR over 1 mL/kg/day was collected. Information regarding stool frequency, time to passage of first stool (age in days), gestational age, APGAR-score, sex, birth-weight and time to NEC diagnosis was also recorded. All parameters were collected from the day of birth until the day of NEC diagnosis in the NEC group. In the control group, data was collected from day of birth and 30 days forth. Average days to NEC diagnosis was 13 days in the NEC group. We decided to analyze data from the 13th day of life and 6 days prior in the control group. In the NEC group data was analyzed from day of NEC diagnosis and the previous 6 days, to see if we could detect any changes in these parameters that could relate to early manifestations of the disease.

**Ethics**

Ethical permission was obtained by the Regional ethical review board in Gothenburg, DNR 319-12. Data included in GAS was daily obtained with routine on all infants who were cared for at the NICU at the time of the study. The parameters were obtained from the patients’ medical records without any discomfort for the patient.

**Analysis**

Statistical analyses were made using Microsoft Excel for Mac 2011 version 14.3.0. and IBM SPSS statistics version 22. Microsoft Excel for Mac 2011 version 14.3.0 was used for creating figures and tables. Non-Parametric Mann Whitney U test was used for statistical comparison of groups. Fishers’s test was used for statistical analysis of mortality rates. Analysis was based on 39 samples for the NEC group and 44 samples for the control group.
Results

The NEC group consisted of 39 infants, 20 males and 19 females, and the control group 44 infants of which 23 were male and 21 female. All infants included in the study were born before gestational week 28+0. Ten patients included in the study died during their neonatal period, 9 patients died of NEC and associated sepsis and 1 patient of sepsis and respiratory failure. NEC mortality was 23.1%. As shown in table 2 there were no significant differences between the groups regarding gestational age, birth weight or sex.

<table>
<thead>
<tr>
<th>Category</th>
<th>NEC group (n=39)</th>
<th>Control group (n=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA w mean ±SD</td>
<td>25.0 ± 1.3</td>
<td>25.4 ± 1.3</td>
<td>ns</td>
</tr>
<tr>
<td>BW g mean ±SD</td>
<td>770.4 ± 183</td>
<td>818.6 ± 213.5</td>
<td>ns</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>20/19</td>
<td>23/21</td>
<td>ns</td>
</tr>
<tr>
<td>Days to passing of first stool mean ±SD</td>
<td>4 ± 2.3</td>
<td>2.9 ± 1.8</td>
<td>P=0.012</td>
</tr>
<tr>
<td>Average stools per day</td>
<td>1.8 ± 0.5</td>
<td>3.5 ± 0.4</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>9/39 (23.1%) all</td>
<td>1/44 (2.3%)</td>
<td>P=0.006</td>
</tr>
<tr>
<td></td>
<td>NEC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Days to passing of first stool was 4 ± 2.3 days in the NEC group and 2.9 ± 1.8 days in the control group which was a significant difference (Table 2). 3 patients in the NEC group did not have passage of meconium before diagnosis.

As seen in figure 1, a significant difference was seen in average stools per day from NEC diagnosis and the 6 previous days compared to day of life 7-13 in controls. Average stools per day in the NEC group were 1.8 ± 0.5 and 3.5 ± 0.4 in the control group.
APGAR score was comparable between the two groups as seen in table 3.

**Table 3. APGAR score**

<table>
<thead>
<tr>
<th>Mean APGAR score</th>
<th>1 minute</th>
<th>5 minutes</th>
<th>10 minutes</th>
</tr>
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<tbody>
<tr>
<td>Case</td>
<td>5</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>P-value</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

Mean total gastric residual volume (GRV) in the NEC group was 4.3 ± 1.3 mL, with a peak 2 days prior to diagnosis and a following decrease, and 5.8 ± 0.6 mL in the control group (figure 2). A significant difference regarding total GRV was seen 5 and 6 days prior to diagnosis as seen in figure 2. Mean total GRV divided by birth weight showed a higher GRV (mL)/kg in the control group (7.5 ±0.7 ml/kg) than in the NEC group (5 ± 1.8 ml/kg), a significant difference was observed 5 and 6 days before diagnosis (figure 3). Figure 4 shows GRV as a percentage of feeds where mean GRV
as a percentage of feeds per day were 8.6% in the control group and 25.1% in the NEC group. There was no significant difference regarding GRV as a percentage of feeds between the 2 groups as seen in figure 4.

Figure 2

Figure 2. Mean total GRV per day in the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life. Data were plotted as mean +/- standard deviation (SD), and the statistical method used was Mann-Whitney U test.
Figure 2

**Mean total gastric residual volume/ Birth weight**

![Graph showing mean total gastric residual volume per birth weight.](image)

Figure 3. Mean total gastric residual volume (mL) divided by birth weight (kg). In the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life. Data were plotted as mean +/- standard deviation (SD), and the statistical method used was Mann-Whitney U test.

Figure 3

**Gastric Residual Volume as percentage of Feeds**

![Graph showing gastric residual volume as percentage of feeds.](image)

Figure 4. GRV as percentage of feeds in the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life. Data were plotted as mean +/- standard deviation (SD), and the statistical method used was Mann-Whitney U test.
As seen in figure 5, average feeds per day, a downward trend can be seen regarding enteral feeds in the NEC group 3 days prior to diagnosis. In the control group, a steady increase in feeding volume can be seen. A significant difference in enteral feeds was seen at day of diagnosis and 2 days prior as seen in figure 5.

GAS is composed out of 4 parameters, as seen in table 1; stool frequency, number of GR >1mL/kg/meal, change of feeds since previous day and amount of enteral feeds (mL) either as intermittent bolus feeds or continuous enteral feeds. Scoring was distributed as seen in table 1, where a score ranging from 0-2 could be distributed for each parameter with a total of maximum 8 points/day/infant, which means that 0 points would indicate that the patient is having frequent stools, GR <1mL/kg/meal, is getting full meals (full meals considered to be >150 mL/kg/day after the first week of

Figure 5. Average feeds per day (mL) from day of diagnosis and 6 days prior in the NEC group and from the 7th-13th day of life (DoL) in the control group. Data were plotted as mean +/- standard deviation (SD), and the statistical method used was Mann-Whitney U test.

<table>
<thead>
<tr>
<th>Days</th>
<th>Average enteral feeds per day NEC group</th>
<th>Average enteral feeds per day control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEC-6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEC-5</td>
<td></td>
<td></td>
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<tr>
<td>NEC-4</td>
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<tr>
<td>NEC-3</td>
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<td>NEC-2</td>
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<td></td>
</tr>
<tr>
<td>NEC-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnos</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 4
life) and that the patient is receiving increased enteral feeds since the previous day. It was seen that the NEC group had a higher score in total compared to the control group. The control group received a total GAS score between 1.7 and 2.4 during the studied period. The NEC group received a total GAS score between 2.3 and 4.5 during the studied period and it was also seen that the score increased closer to day of NEC diagnosis with the highest score on the day of diagnosis. Scores in the NEC group consistently increased leading up to day of diagnosis except the score for GR that instead decreased as displayed in figure 6.

**Figure 5**

<table>
<thead>
<tr>
<th>Gothenburg Abdominal Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>7.5</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>6.5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>5.5</td>
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<tr>
<td>5</td>
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<tr>
<td>4.5</td>
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<td>4</td>
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<td>3.5</td>
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<td>1</td>
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<tr>
<td>0.5</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

Figure 6. Gothenburg Abdominal scoring. NEC group scores from day of NEC diagnosis and 6 days prior. Control group scores from the 7th-13th day of life (DoL), scoring according to GAS.

Figure 7, 8, 9 and 10 displays diagrams showing the individual components of the GAS system.
Figure 6

**GAS - Stool frequency**

![Graph showing stool frequency score over days.](image)

- **GAS - Stool frequency**
  - **Score**
  - Days include NEC-6, NEC-5, NEC-4, NEC-3, NEC-2, NEC-1, NEC Diagnosis.
  - **NEC group** and **Control** are compared.

**GAS - Gastric residuals**

![Graph showing gastric residuals score over days.](image)

- **GAS - Gastric residuals**
  - **Score**
  - Days include NEC-6, NEC-5, NEC-4, NEC-3, NEC-2, NEC-1, NEC Diagnosis.
  - **NEC group** and **Control** are compared.

---

**Figure 7.** Scoring of stool frequency according to GAS. In the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life.

**Figure 8.** Scoring of gastric residuals according to GAS. In the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life.
Figure 8

GAS - Enteral feeds

Figure 9. Scoring of enteral feeds according to GAS. In the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life.

Figure 9

GAS - Change of feeds since previous day

Figure 10. Scoring of change of feeds since previous day according to GAS. In the NEC group from day of diagnosis and 6 days prior and in the control group from the 7th-13th day of life.
Discussion

The aim of this study was to determine if the Gothenburg Abdominal Scoring could be used as a way to detect NEC earlier in preterm infants. The present study shows that scoring increased in the NEC group 4 days before diagnosis with the highest score on the day of diagnosis. The parameters that were most distinguished were *enteral feeds, stool frequency and change of feeds since previous day* whereas *gastric residuals* had very little predictive value for NEC development.

Furthermore, this study shows that preterm infants born before gestational week 28+0 who develop NEC have a significantly lower frequency of stool during the 6 days prior to NEC diagnosis compared to controls. The report also shows that the NEC group had a delayed passage of first stool. This suggests that the bowel is somewhat already compromised in infants who develop NEC and that these findings cannot only be seen as an effect of prematurity. Most term infants pass their first stool within their first 2 days of life. In a study composed by Bekkali et al. infants with a BW <1500 g had a mean duration of passage of meconium of 7.8 days. Also, they found that the duration of passing of meconium was delayed further by each week of prematurity and if they received morphine therapy [16]. Other factors Bekkali et al. found to have significance when it came to passing of meconium was respiratory support and TPN[16]. TPN might cause delay because of the importance of enteral feeds for the development of the GI-tract[2]. A question concerning the ability to hasten the passing of meconium and the transition to normal stools appears. According to Haiden et. al. and Shim et. al., the use of different enema strategies have shown that feeding tolerance can be promoted and full enteral feeds can be reached faster but also that NEC could be a possible consequence using these methods[15, 18]. Stool pattern was found different in this study compared to the previous study by Andrews et
al.[21]. As preterm infants have an immature gut it would seem that the findings in this study, that preterm infants diagnosed with NEC have a lower stool frequency compared to healthy controls, are plausible since both the ability to absorb nutrition and the ability to expel waste is inadequate.

However, it is unclear whether or not any of the parameters included in GAS can be seen as alarm symptoms for NEC, but a trend could be seen during the days leading up to NEC diagnosis in the studied group. It was seen that the score for *enteral feeds* and *change of feed since previous day* started to increase two days before diagnosis. This was significant for the studied group in whole but the relevance for the individual infant is more difficult to interpret.

Gastric residuals has been a much discussed topic when it comes to NEC but in this material we could not see a significant difference of total gastric residual volume per day compared to controls. GRV appears not to be a good predictor of NEC.

As NEC is a disease of the premature infant it is clear that the undeveloped bowel has a part in the disease manifestation but looking to this material there must also be other factors in play. More studies concerning the premature infant GI-tract development is needed as to get a clearer picture of what triggers and causes the disease to manifest. From there better strategies on how to handle early NEC development need be formed.

**Limitation of study**

NEC is a rare condition, which means that the data for the NEC group was obtained during a long period of time, 2004-2014. It would have been better if
the studied subjects had been born during the same time period and to have had been able to pair each NEC infant with a control.

Another issue with the collected data was that it was entered manually which could lead to discrepancies when filled out by different nurses and also for myself when interpreting the medical records.

**Conclusion**

NEC patients born before gestational age 28+0 have a significantly delayed passage of meconium and significantly lower frequency of stools prior to NEC development compared to controls. It is unclear if this contributes to the development of NEC, or if it is an indication of an already compromised gut. Frequency and volume of gastric residuals seems not to precede NEC development. An increase in GAS score was seen in the NEC group days before diagnosis. A significant difference was seen in enteral feeds and stool frequency for the group in whole but the relevance for the individual patient remains uncertain.

**Populärvetenskaplig sammanfattning**

Nekrotiserande enterokolit (NEC) är en av de mest fruktade sjukdomar som drabbar för tidigt födda barn. NEC är en akut inflammatorisk tarmsjukdom med hög dödlighet och sjuklighet där värdet av att ställa en tidig diagnos är oerhört viktig för utfallet. Idag finns inget specifikt test för att ställa denna diagnos vilket gör att insatser för att förhinder sjukdomens uppkomst eller fortskridande inte alltid sätts in i tid. Idag baseras diagnosen på röntgenbilder på tarmarna, laboratorieprover och klinisk undersökning av barnet. De prover man tar kan tydligt visa på en pågående
Fortsättningsvis är det viktigt att fortsätta undersöka faktorer som kan tänkas trigga igång sjukdomen för att kunna utveckla bättre metoder som tidigarelägger diagnosen NEC.

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