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Surgery for intestinal injuries in very preterm infants: a Norwegian population-based study with a new approach to disease classification

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ABSTRACT

Objective To evaluate population-based data on very preterm infants (<32 weeks gestation) operated for intestinal injuries, focusing on necrotising enterocolitis (NEC) and focal intestinal perforation (FIP).

Design Nationwide, population-based registry cohort study.

Setting All 21 neonatal units in Norway.

Participants All very preterm infants born from 2014 through 2021 and admitted to a neonatal unit.

Main outcome measures Incidence of surgery for subgroups of intestinal injuries, medical record data on laboratory-radiology results, anatomical location of affected bowel, length of resections, number of re-operations, morbidities of prematurity and/or death before discharge.

Results Abdominal surgery was performed in 124/4009 (3.1%) very preterm infants and in 97/1300 (7.5%) extremely preterm infants <28 weeks. The main intestinal injuries operated were NEC (85/124; 69%), FIP (26/124; 21%) and 'other abdominal pathologies' (13/124; 10%). NEC cases were divided in (i) acute NEC, extensive disease (n=18), (ii) non-extensive disease (n=53) and (iii) NEC with surgery >3 days after disease onset (n=14). High lactate values immediately prior to surgery was predominantly seen in acute NEC-extensive disease and associated with high mortality. Other laboratory values could not discriminate between acute NEC and FIP. Timing of surgery for acute NEC and FIP overlapped. Radiological absence of portal venous gas was typical in FIP. Most infants (62.5%) underwent a stoma formation at initial surgery. The overall survival rate was 67% for NEC and 77% for FIP.

Conclusion NEC cases have different presentation and prognosis depending on the extent of bowel affected. Revised classifications for intestinal injuries in preterm infants may improve prognostication and better guide therapy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The definition of necrotising enterocolitis (NEC) has evolved over time resulting in multiple definitions based on a wide range of diagnostic criteria.
⇒ Distinguishing NEC and focal intestinal perforation (FIP) is challenging.

WHAT THIS STUDY ADDS

⇒ NEC has very different prognosis depending on extent of bowel affected.
⇒ Timing of surgery for acute NEC and FIP overlapped in this study.
⇒ Portal venous gas was not observed in FIP cases, but associated with high mortality in NEC cases.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This population-based study supports attempts to revise classification of neonatal intestinal injuries to improve prognostication and better guide future therapy.

BACKGROUND

The immature gastrointestinal tract in very preterm (VP; <32 weeks gestation) infants is prone to injuries. Improvements in care have resulted in an increasing number of VP infants with intestinal injuries that survive to surgery.[1 2] Necrotising enterocolitis (NEC) is the most common surgical emergency in VP infants, but focal intestinal perforation (FIP) and other intestinal injuries are difficult to distinguish from NEC due to similar clinical presentations.[3 4] Furthermore, NEC is no longer considered a distinct entity, but more likely consists of different subgroups of intestinal injuries.[5]

Surgical intervention for intestinal injuries carry a substantial risk for mortality and morbidity in VP infants.[6 7] Surgery and exposure to general anaesthesia are associated with impaired neurodevelopmental outcome.[8 9] Determining indications and optimal timing of surgery is challenging.[10] Early surgery may reduce ongoing deleterious cascades of inflammation affecting the brain and the

Table 1 Baseline characteristics of the study cohort

Abdominal surgery GA <28 weeks, n (%)	Acute NEC Non-extensive disease N=53 41 (77.4%)	Acute NEC Extensive disease N=18 16 (88.9%)	NEC Later surgery N=14 13 (92.9%)	Acute FIP N=26 18 (69.2%)	Other abdominal pathologies N=13 9 (69.2)
GA (weeks)	25.0 (23.6–27.5)	25.5 (24.3–27.4)	25.6 (24.1–26.6)	26.5 (24.3–28.8)	26.1 (25.3–28.8)
Birth weight (g)	666 (573–895)	776 (588–923)	755 (604–871)	752 (606–1076)	735 (624–960)
Birth weight Z-score	−0.59 (−1.25 to −0.16)	−0.74 (−1.61 to 0.09)	−0.64 (−1.12 to −0.03)	−1.04 (−1.93 to −0.21)	−0.95 (−1.91 to −0.79)
SGA, n (%)	12 (23)	5 (28)	2 (14)	10 (40)	5 (39)
Female, n (%)	24 (45)	7 (39)	9 (64)	12 (46)	6 (46)
Plurality (%)	18 (34)	4 (22)	3 (21)	8 (32)	5 (39)
Antenatal steroids, n (%)	50 (94)	18 (100)	13 (93)	26 (100)	13 (100)
Apgar score at 5 min	7 (6–9)	6.5 (6–9)	7 (6–9)	8 (6–8)	8 (7–9)
CRIB2	14 (10–16)	12 (9–15)	11 (10–15)	12 (8–14)	11 (9–14)
Age (days) at first surgery	10 (7–18) 2, 44	11 (7–21) 3, 37	40 (25–50) 22, 78	5 (4–12) 3, 39	12 (3–26) 1, 58
Weight (g) at first surgery	762 (583–967)	758 (700–920)	1198 (912–1680)	813 (600–1050)	940 (692–1102)
PMA at first surgery (weeks)	27.1 (25.3–29.6)	27.0 (25.5–30.6)	30.8 (28.1–33.5)	27.4 (25.5–29.7)	29.1 (26.3–31.1)

Data are presented as median (IQR), and also range (age first surgery).
Day of birth is day zero.
CRIB2, clinical risk index for babies 2; FIP, focal intestinal perforation; GA, gestational age; NEC, necrotising enterocolitis; PMA, postmenstrual age; SGA, small for gestational age.

circulation. However, postoperative complications such as stoma problems, metabolic disturbances and poor growth are common.[11]

Despite advances in neonatal care, questions remain unanswered regarding diagnostic considerations, decisions around surgical and medical management and overall prognosis for VP infants operated for intestinal injures. Many publications include patients 'broadly' classified as having either NEC or FIP from large register studies[12–14] or include selected cohorts from tertiary centres[3 6 15–18] carrying a risk of both imprecise classification of intestinal injuries and selection bias. In this study, we report contemporary, population-based data on all VP infants in Norway who over an 8-year period underwent abdominal surgery during admission in the neonatal intensive care unit (NICU). We aim to classify intestinal injuries in different entities, and to evaluate presentation and prognosis, by combining clinical data with laboratory, radiological, intraoperative and pathology findings.

MATERIALS AND METHODS

Setting and study design

This is a population-based study with data from the Norwegian Neonatal Network (NNN), supplemented with extracted data from the patient medical records. We included all VP infants born from January 2014 through December 2021 and who had undergone abdominal surgery before discharge from the NICU. Neonatal surgery in Norway is centralised to two centres, but infants may have surgery in other units based on availability of local competence and the severity of acute, critical illness. Eligible infants were identified in the NNN database. For completeness, we also searched this database for all infants who were diagnosed with NEC and who died, without having surgery. All parents received written information about the study, describing that, in addition to routine registry data, data from electronical medical records, surgery notes and pathology reports were retrieved. The latter data were not collected if parents opted out.

Study data

Registry data included birth weight (BW), gestational age (GA), small for GA (BW <10 percentile),[19] clinical risk index for babies 2,[20] Apgar score, plurality, sex, antenatal steroid exposure, weight at 34 weeks postmenstrual age, discharge diagnoses and mortality before discharge from the NICU. Medical record data were based on a template by Berrington and Embleton[21] with some modifications. We report last laboratory values obtained before surgery and positive blood cultures obtained within ±2 days of surgery. Radiology data include plain abdominal radiography and ultrasound examinations, focusing on reported pneumoperitoneum, pneumatosis intestinalis or portal venous gas (PVG). Length of the bowel resected was estimated from surgical notes or histology reports. Duration (days) of nil by mouth was defined as time in days from when enteral nutrition was stopped presurgery until recommenced postsurgery, whereas time to full feeds included the time from when feeds were recommenced postsurgery until a daily volume of 150 mL/kg/day was reached.

Definitions of intestinal injury

We classified intestinal injuries based on a combination of clinical data, surgery notes and pathology reports. Cases were classified as acute FIP if there were ≤2 bowel perforations and no obvious sign of surrounding bowel necrosis or inflammation. Cases classified as NEC were characterised by signs of thickened, inflamed or necrotic bowel wall during surgery and/or pathology reports

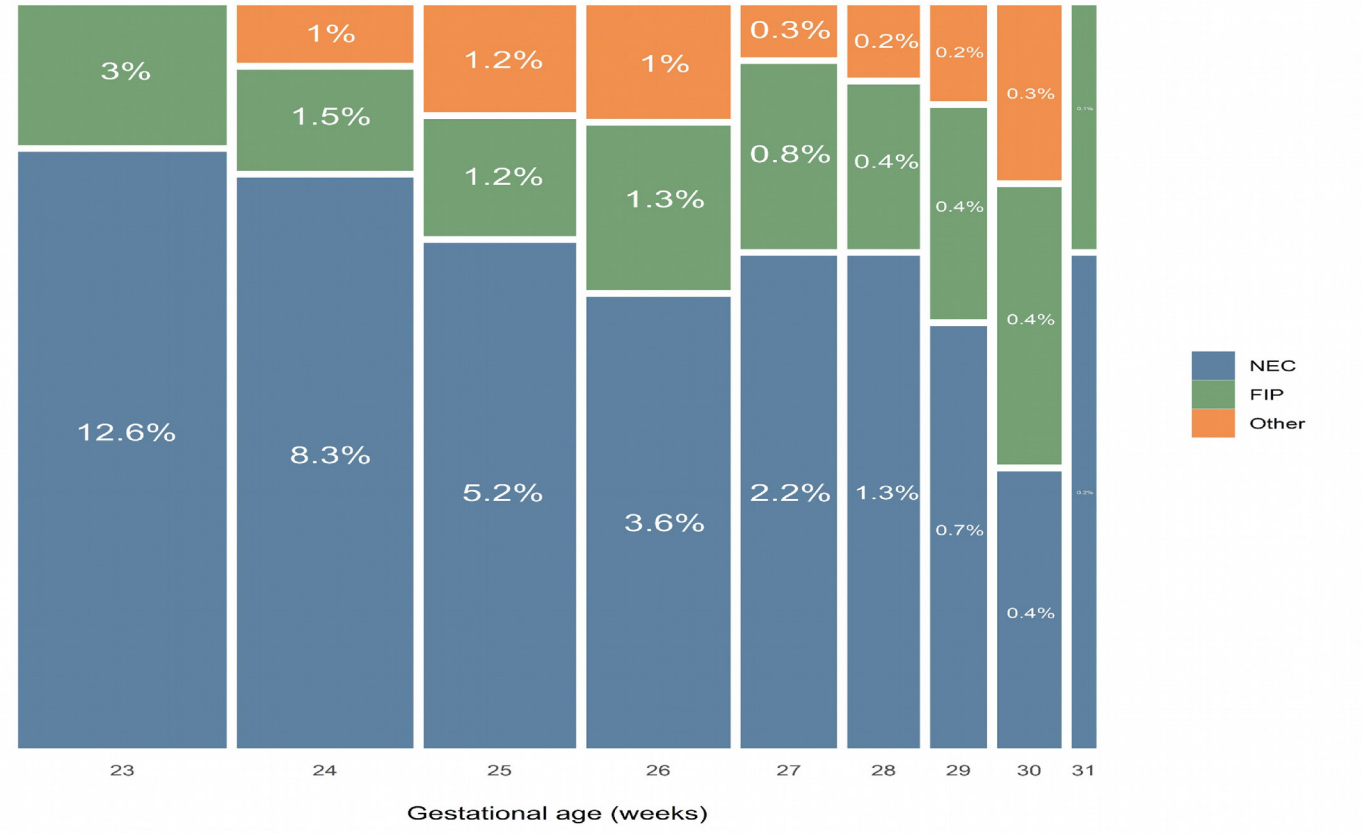

Figure 1 Mosaic plot with incidence of abdominal surgery from 23 to 31 weeks of gestation at birth. FIP, focal intestinal perforation; NEC, necrotising enterocolitis.
Note for gestational age 31 weeks NEC rate is 0.2% and FIP rate 0.1%

describing signs of necrosis and inflammation. We defined three different NEC 'subclasses': (i) acute NEC, non-extensive disease, (ii) acute NEC, extensive disease (residual postoperative small bowel length <30 cm)[22] and (iii) NEC with later surgery (>3 days after onset of the acute disease course). The remaining cases undergoing surgery were classified as 'other abdominal pathologies'.

Outcomes

The main outcome measures were the incidence of surgery for all subgroups of intestinal injuries, overall mortality before discharge and for those with a diagnosis of NEC or FIP, we also evaluated preoperative laboratory and radiology results, anatomical location of affected bowel, length of bowel resections, number of re-operations and associated morbidities of prematurity.

Patient and public involvement

We presented and discussed our research plans with representatives from the Norwegian Prematurity Association in Stavanger in August 2018 before embarking on this project. However, they were not directly involved in the design, conduct or reporting of this registry study. The results will be disseminated in the journal of the Norwegian Prematurity Association.

Statistical methods and ethics

Data were analysed using IBM SPSS Statistics for Windows, V.29.0. Descriptive data are expressed as median and IQR, with minimum and maximum values where appropriate. Differences between groups were analysed using non-parametric tests for continuous variables and the χ^2 test for categorical data. P-values <0.05 were considered statistically significant.

RESULTS

Among 4009 VP infants born in Norway during the 8-year study period, 124 (3.1%) underwent abdominal surgery. In the subgroup of 1300 extremely preterm (EP; GA <28 weeks) infants, 97 (7.5%) underwent abdominal surgery. Surgery was performed in the two neonatal surgical centres for 92 infants (74%) and the remaining 32 infants (26%) were operated in two other centres. In the NNN database, an additional 10 infants had NEC as reported cause of death during the study period but did not undergo any surgery (online supplemental figure 1).

The parents of five infants opted out of letting researchers review their infant's medical records. We therefore have background NNN registry data for 124 infants (table 1) and more detailed peri-operative and postoperative data from 119 infants. We classified 69%

Table 2 Comparison of pre-operative findings in 93 cases of acute NEC and FIP

	Acute NEC; non-extensive disease (n=52)	Acute NEC; extensive disease (n=16)	Acute FIP (n=25)	P value*
Gastrointestinal symptoms				
Gastric residuals	24 (46)	8 (53)	17 (68)	0.30
Vomiting	4 (8)	2 (13)	5 (20)	0.34
Bilious aspirate	21 (40)	3 (20)	12 (48)	0.19
Bloody stools	5 (9)	1 (7)	1 (4)	0.63
Distended abdomen	40 (76)	15 (100)	20 (80)	0.18
Discoloured abdomen	22 (42)	6 (40)	11 (44)	0.95
Tender abdomen	13 (25)	2 (13)	4 (16)	0.41
Laboratory†				
C reactive protein (mg/L)	43 (10–83)	20 (4–28)	19 (3–71)	0.25
White blood cells ($\times 10^6$/L)	11.2 (5.7–20.5)	13.9 (7.4–25.8)	11.4 (6.6–21.6)	0.63
Platelets ($\times 10^9$/L)	112 (47–170)	193 (47–306)	124 (72–175)	0.51
pH	7.22 (7.16–7.30)	7.06 (6.95–7.20)	7.22 (7.14–7.27)	0.003
Base deficit (mmol/L)	6 (4–10)	15 (11–21)	7 (4–9)	<0.001
Na (mmol/L)	136 (129–141)	135 (128–138)	135 (131–143)	0.46
Lactate (mmol/L)	1.9 (1.3–4)	8.0 (4.3–12)	1.9 (1.2–3.1)	<0.001
Positive blood culture‡	18 (35)	5 (31)	3 (12)	0.11
Radiology				
Abdominal X-ray taken	52 (100)	16 (100)	25 (100)	
Pneumoperitoneum	27 (52)	7 (44)	20 (80)	0.030
Pneumatosis intestinalis	11 (21)	7 (44)	1 (4)	0.009
Portal venous gas	5 (10)	8 (50)	0	<0.001
Abdominal ultrasound taken	39 (75)	11 (69)	16 (64)	0.41
Pneumatosis intestinalis	18 (46)	6 (55)	4 (25)	0.021
Portal venous gas	9 (23)	7 (64)	0	<0.001
Thickened bowel wall	10 (26)	2 (18)	3 (19)	0.057
Ascites	28 (72)	8 (73)	13 (81)	0.054
Absent peristalsis	21 (54)	6 (55)	6 (38)	0.039

All data are median (IQR) or numbers (%), if not otherwise stated.
A total of 97 acute NEC and FIP cases were included with background data in this study, but four caregivers opted out of the medical chart review, thus only 93 patients were included here.
*Statistical comparison between the three groups using Kruskal-Wallis test or χ^2 test, as appropriate.
†If laboratory values were not obtained within 24 hours before surgery, they were not reported.
‡Blood culture: NEC; 13 Gram-negative and 10 Gram-positive bacteria. FIP; 2 Gram-negative and 1 Gram-positive bacteria.
FIP, focal intestinal perforation; NEC, necrotising enterocolitis.

of the operated infants with NEC (85/124) and 21% with FIP (26/124), giving an overall incidence of surgery for NEC and FIP of 2.1% and 0.65%, respectively. Another 10% of the infants underwent surgery for other abdominal pathologies (13/124) (online supplemental table 1). Further details on these are not presented.

Most infants with NEC (70/85; 82%) and FIP (18/26; 69%) were EP infants (table 1). Incidence of surgery for NEC and FIP among EP infants were 70/1300 (5.4%) and 18/1300 (1.4%), respectively. Rates of abdominal surgery were inversely related to GA (figure 1). Surgery for NEC was performed during the first week of life in 23/85 (27%) patients; 17 infants with non-extensive disease and 6 infants with extensive disease. In comparison, a larger proportion of infants with FIP (19/26; 73%) had surgery during the first week of life, p<0.0001. For infants who underwent later surgery following NEC, the onset of their NEC symptoms occurred at a median (IQR) age of 12 (10–19) days.

Gastrointestinal symptoms and laboratory findings prior to surgery in patients with acute NEC and FIP are presented in table 2. Distended abdomen and gastric residuals were the most common findings, whereas vomiting and bloody stools were infrequently reported across all groups (table 2). In the last blood samples obtained prior to surgery, we found markedly higher lactate (figure 2A)

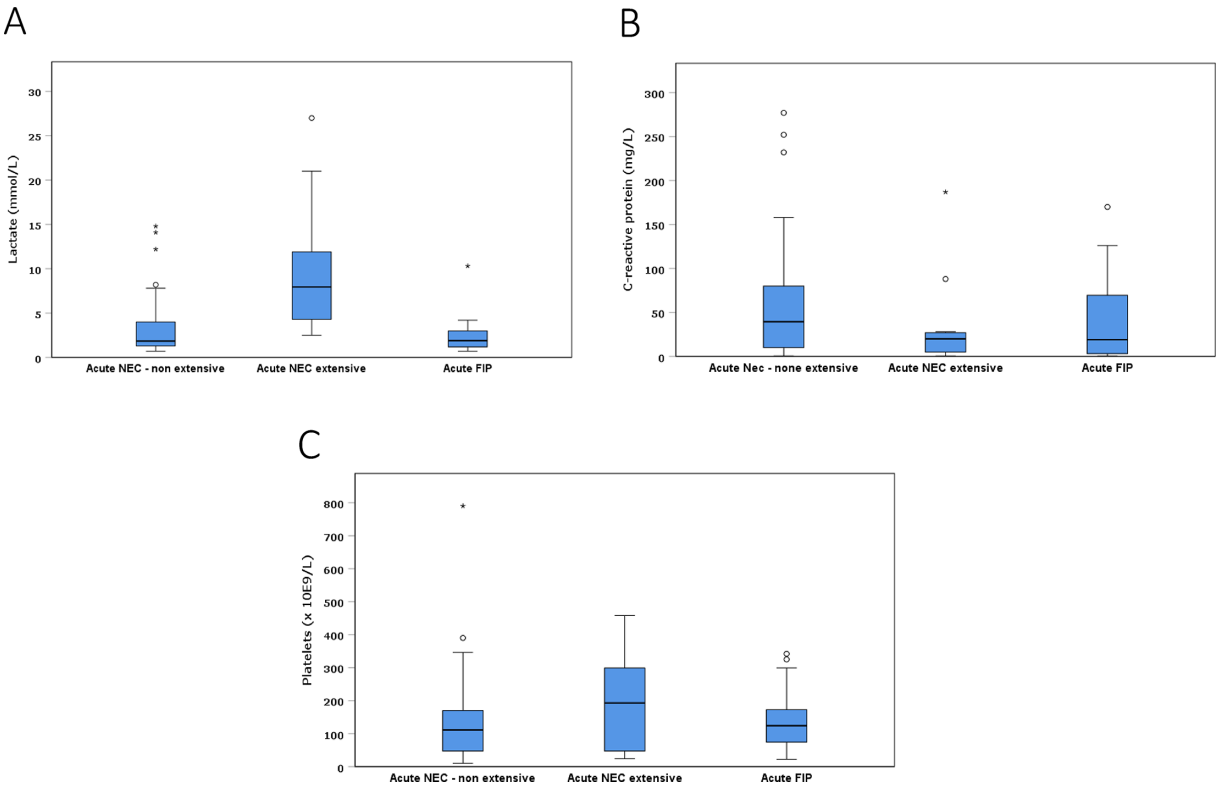

Figure 2 Last laboratory values obtained before surgery for acute NEC (extensive and non-extensive disease) and acute FIP. (A) Lactate (mmol/L). (B) C reactive protein (mg/L). (C) Platelets (10^9/L). FIP, focal intestinal perforation; NEC, necrotising enterocolitis.

and base deficit, with corresponding lower pH, among infants with acute NEC, extensive disease compared with other groups. However, there were no differences in laboratory values, including C reactive protein (CRP) and platelet values (figure 2B,C), prior to surgery among infants with acute NEC, non-extensive disease and FIP. Overall, 23 out of 68 (34%) infants with NEC and 3 out of 25 (12%) infants with FIP had positive blood cultures (table 2). Abdominal radiography and ultrasound examinations were used for diagnostics in most cases (table 2). Pneumoperitoneum was more common in FIP cases, while pneumatosis intestinalis was more common in NEC cases. PVG was not observed in any cases classified as FIP, but was present in 9 out of 18 (50%) infants with NEC who died.

Surgical details and postoperative outcomes for the NEC subgroups and FIP are presented in table 3. One surgical centre performed approximately two-thirds of the operations, and survival rates were similar between centres (data not shown). The overall survival rate was 67% (57/85) for NEC and 77% (20/26) for FIP. In 15/16 (94%) infants with acute NEC and extensive disease, no bowel resection was attempted, and care was redirected. The majority of infants who underwent surgery for NEC/FIP (57/91; 63%) had a stoma formation after the first operation. However, 14/52 (27%) of cases with acute NEC, non-extensive disease and 10/25 (40%) of cases with FIP underwent a primary anastomosis. The 77 infants with NEC and/or FIP who survived to discharge had a total of 201 operations (including re-operations, and stoma closures), with a median (IQR) of 2 (2–3) operations per infant. No infant was treated with a peritoneal drain.

Pathology reports were available in 96/119 (81%) infants. There was no standard format for the reports, many were short and some were challenging to review due to imprecise descriptions. Among the 68 acute NEC cases reviewed in detail, we identified 52 reports describing necrosis and/or inflammation, compatible with NEC. One report was described as FIP but due to perioperative findings reclassified to NEC. In the remaining NEC cases, 4 were not possible to categorise and 11 did not have a pathology report. Among the 26 FIP cases, 18 reports showed lack of necrosis/inflammation, consistent with FIP. In two cases, a perforation was not described, and six cases did not have pathology reports.

DISCUSSION

To the best of our knowledge, this is the first nationwide cohort study reporting on all VP infants operated due to any abdominal pathology. Overall, 3.1% of all VP infants and 7.5% of all EP infants in Norway between 2014 and 2021 underwent abdominal surgery during their NICU stay. Classifying NEC and FIP is complicated by the overlapping clinical presentations and the absence of standardised diagnostic criteria.[3 4 23 24] We subclassified NEC cases undergoing acute surgery as NEC, extensive

Table 3 Surgery and postoperative outcomes

	Acute NEC Non-extensive disease (n=52)	Acute NEC Extensive disease (n=16)	NEC Later surgery (n=13)	Acute FIP (n=25)
Primary surgery				
Primary anastomosis and no stoma	14/52 (27)	N/A	6/13 (46)	10/25 (40)
Stoma formation	37/52 (71)	1/16 (6)	7/13 (54)	12/25 (48)
Other types of surgery*	1/52 (2)	15/16 (94)†		3/25 (12)
Length of estimated bowel resected (cm)	10 (6–24)	†	15 (9–25)	3.4 (2.5–5)
Reoperations after first surgery				
Total numbers of operations (including second look and stoma closure)	51+69=120	1+1=2	13+14=27	25+16 = 41
Days with stoma until closure	96 (69–137), n=37	N/A	101 (63–145), n=5	93 (53–125), n=10
Intestinal injury location				
Small bowel only	36 (69)	7 (44)	12 (92)	17 (68)
Large bowel only	5 (10)	1 (6)	1 (8)	7 (28)
Both small/large bowel	11 (21)	8 (50)	0	1 (4)
Growth and nutrition				
Time (days) nil by mouth	7 (4–11.5)	N/A	11 (1.5–16)	4 (2.5–6.3)
Time (days) to full feed	14 (9–48)	N/A	12 (3–28.5)	9.5 (0.8–15.5)
Weight at PMA 34 weeks (g)	1575 (1317–1879)	N/A	1735 (1534–1936)	1755 (1600–2021)
Outcomes				
Severe ROP among survivors to discharge	14/46 (30)	1/1 (100)	5/11 (45)	4/20 (20)
Severe BPD among survivors to discharge	23/46 (50)	1/1 (100)	7/11 (64)	10/20 (50)
cPVL among survivors to discharge	0/46 (0)	0/1 (0)	3/11(27)	6/20 (33)
Survival to discharge‡	45/53 (85)	1/18 (6)	11/14 (79)	20/26 (77)
Median (IQR) age of death (days)‡	14 (5–76)	11 (8–20)	37 (32–48)	13 (7–28)

All data are n (%) or median (IQR) if not otherwise stated.
The numbers presented are from data available and the total numbers may not always be consistent due to mortality and some incomplete data.

*Three perforation closures in children with acute FIP and one child with acute NEC, non-extensive disease who collapsed during surgery and care was redirected.
†In 15/16 NEC extensive disease, no further surgery was attempted or possible. The last patient had an estimated remaining small bowel length of 23 cm.
‡Numbers on survival and age of death relates to all 124 patients included in the study.
BPD, bronchopulmonary dysplasia; cPVL, cystic periventricular leukomalacia; FIP, focal intestinal perforation; N/A, not available or applicable; NEC, necrotising enterocolitis; PMA, postmenstrual age; ROP, retinopathy of prematurity.

and non-extensive disease, and these two groups had a different presentation and prognosis. Despite the lack of standardisation, pathology reports were useful to differentiate NEC and FIP.

Comparing the incidence of surgical NEC and FIP between countries and networks is challenging due to variations in reports regarding the GA/BW of the infants included, and selected populations. According to our classification, 2.1% of all VP infants had surgery due to NEC and 0.65% due to FIP. These numbers are slightly lower than reports on surgery for NEC and FIP among very low BW infants (<1500 g) in the USA (NEC 3.1% and FIP 1.6%)[25 26] and Germany (NEC 3.6% and FIP 1.7%).[27] In Sweden, the rate of surgery for NEC was 5.3% among infants with GA <27 weeks in 2014–2016. This rate is similar to the rate among infants with GA <28 weeks in our cohort (5.4%).[1]

In our cohort, the median age at surgery for FIP was earlier than for NEC. However, postnatal age at surgery overlapped and one-fourth of the NEC infants had surgery in the first week of life.[21 23] In line with others, we found severe lactacidosis in neonates with extensive NEC, and others also report that severe lactacidosis is associated with high mortality.[28] Other laboratory parameters including CRP and platelet values did not appear to be useful for discriminating acute FIP versus acute NEC non-extensive disease. Abdominal ultrasound was used as a diagnostic tool in most cases, in contrast to data from a recent Swedish study where only 19% of surgical NEC cases had been examined with abdominal ultrasound.[14] None of the infants operated for FIP had signs of PVG, in line with other reports showing that PVG is sensitive and specific for NEC.[29 30] Presence of PVG in our study was associated with extensive NEC and poor prognosis, as also reported by others.[14 31]

The classical FIP case is described as a single 'blow-out lesion', typically in the terminal ileum.[32 33] However, in our cohort, 28% of infants with FIP had exclusive involvement of the large bowel, more than 13%–17% previously reported.[21 34] For several reasons, the anatomical location of the perforation in FIP is not always reported. This may be explained by lack of surgical details in large registry studies and because conservative management with percutaneous drainage is a common approach in some countries.[26]

Stoma formation is common practice after abdominal surgery[10 14 34 35] and was the predominating surgical choice in our cohort regardless of underlying condition. Still, around one-fourth of all infants with NEC, non-extensive disease and 4/10 infants with FIP were managed with a primary anastomosis. In a recent large study of infants with NEC, only 15.8% were managed with a primary anastomosis after intestinal resection, showing no difference in outcomes to those with a stoma.[36] Our study was too small to study differences between the groups, but shorter duration of parenteral nutrition and less hyponatraemia has been suggested as potential advantages of a primary anastomosis.

Mortality rates from surgical NEC varies from 30% to 60%, and is highest in EP infants.[37] However, lack of an agreed definition of NEC and lack of granular data on whether mortality is directly attributable to NEC or not, hampers comparisons of mortality between studies.[3 18 23] We found that only 1 out of 16 infants with documented NEC and extensive disease survived. This baby was offered long-term parenteral nutrition. In contrast, mortality rate in NEC with non-extensive disease was only 15%, which is an important finding when counselling parents about prognosis. A FIP mortality rate of 23% in our study is comparable with other reports.[26 38] In the future, a revised classification of intestinal injuries may lead to identification of subentities of intestinal injuries with more specific prognosis enabling a more tailored intervention. Indeed, a large US study using unsupervised machine learning identified five clusters of intestinal injury, including one deemed the 'low mortality' cluster and another deemed the 'immature with high mortality' cluster.[24]

The major strength of this study is the population-based design including all VP infants who underwent abdominal surgery in Norway over an 8-year period. We excluded medical NEC cases for which uncertainty exists around the diagnosis.[23 39] We performed a detailed review of all cases, which secures better data quality and granularity compared with pure registry studies.[3 14 26 27] Our study also has several limitations. First, an inherent bias with retrospective chart reviews is that some data were missing or hard to interpret, for example, some radiology and pathology reports, and we were not allowed to review the medical chart in five patients. Second, our classification of intestinal injuries is prone to bias. We scrutinised the medical charts but cannot rule out that some FIP/NEC cases may have been misclassified. Third, the reported estimated length of resected bowel was from either surgery notes or pathology reports, and disparate lengths are reported.[40] Moreover, remaining bowel length was only reported for NEC, extensive disease cases when this was specifically mentioned in the surgical notes. Finally, despite investigating all VP infants in Norway over an 8-year period, the number of infants included is low and this limits statistical comparisons between groups.

In summary, this study documents that NEC may have a very different presentation and prognosis depending on the extent of bowel affected. Moreover, there is a clear overlap in timing of surgery for NEC and FIP, even though FIP predominantly presents in the first week of life. Laboratory values have a limited value in discriminating between different intestinal injuries. Absence of radiological signs of PVG is typical in FIP. Overall, new classification systems for intestinal injuries in preterm infants are needed to better guide future therapy. In line with others,[3 21] we suggest that future clinical and observational trials include all (premature) infants who have undergone abdominal surgery including clinical, surgical and histological outcome data in order to allow better understanding of neonatal intestinal injuries.

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for the overall content and guarantor of this study. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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