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The outcome of critically ill neonates undergoing laparotomy for necrotising enterocolitis in the neonatal intensive care unit: a 10-year review

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ABSTRACT

Purpose: To evaluate outcomes in critically ill neonates with necrotising enterocolitis (NEC) undergoing a laparotomy in the neonatal intensive care unit (NICU).
Methods: This is a retrospective review of neonates diagnosed with NEC who underwent a laparotomy on NICU between 2001 and 2011. Demographic, diagnostic, operative and outcome data were analysed. Nonparametric comparison was used. Data are reported as median (range).
Results: 221 infants with NEC were referred for surgical evaluation; 182 (82%) underwent surgery; 15 (8%) required a laparotomy on NICU. Five had NEC totalis, 4 multifocal disease and 6 focal disease. Five had an open and close laparotomy, 8 stoma with/without bowel resection and 2 bowel resection and primary anastomosis. Ten (67%) died at a median of 6.5-hours (2–72) postoperatively; 2 died at 72 and 264-days. The 30-day mortality rate was higher ($p = 0.01$) among infants undergoing a laparotomy on NICU (10/15; 67%) than in theatre (54/167; 32%). There was no significant difference in mean Paediatric Index of Mortality 2 Scores between survivors and nonsurvivors ($p = 0.55$). Three (20%) infants remain alive with no or minimal disability at 1.4 (0.5–7.5) years.
Conclusion: Laparotomy for NEC on NICU is a treatment option for neonates who are too unstable to transfer to theatre. However, with 67% dying within 6.5-hours and a further 13% after months in hospital, we must consider whether surgery is always in their best interests. Development of a prediction model to help distinguish those at highest risk of long-term morbidity and mortality could help with decision making in this difficult situation.

Necrotising enterocolitis (NEC) is a devastating disease primarily affecting the premature neonate and is associated with significant morbidity and mortality [1–3]. The mainstay of treatment is medical, involving administration of broad-spectrum antibiotics and cessation of enteral feeds. However, when medical treatment fails, or complications supervene, surgery is invariably required. Surgical interventions have included peritoneal drainage or laparotomy; the latter may involve a number of surgical procedures including resection of necrotic/gangrenous bowel accompanied by either a primary anastomosis or stoma [4].

Infants presenting with advanced NEC disease often require inotropes and high frequency oscillation ventilation (HFOV) for cardiorespiratory support. These infants are sometimes too critically unstable to be safely transferred to the operating theatre (OT), especially if the OT is on a different floor [5–8]. In such situations, the laparotomy may be carried out in the neonatal intensive care unit (NICU).

Previous studies have reported outcomes of surgical procedures undertaken on NICU versus the OT, primarily patent ductus arteriosus (PDA) closure [5–9]. They have shown a higher mortality rate in the NICU group related to underlying prematurity, illness and anomalies, but not the operative location. However, there is limited information available on the mortality and long-term morbidity of critically ill/unstable neonates operated on NICU for NEC. In this study, we aimed to evaluate outcomes of neonates with NEC undergoing a laparotomy on NICU over a 10 year period in order to provide information to help surgeons, neonatal intensivists and the families of these sick neonates make very difficult decisions about surgical intervention.

1. Methodology

1.1. Study design

We obtained ethical approval for a retrospective case note review of all neonates with a diagnosis of NEC who underwent a laparotomy for NEC in the NICU at Great Ormond Street Hospital for Children

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(GOSH) from 31st May 2001 to 1st June 2011. NEC was diagnosed using Bell's Staging system, as modified by Kleigman [10,11]. Cases were identified through two searches of the hospital computerised clinical coding database: 1) of all the neonates with a diagnosis of NEC and who had undergone a laparotomy, 2) of all neonates with NEC who died within 24 hours of admission to NICU. Electronic NICU discharge summaries were searched to identify if and where (OT or NICU) the laparotomy was undertaken. If not clearly documented the case notes were retrieved and searched for this information. Of all those fulfilling the study criteria, data were retrieved by two authors (NJW, MT) from the case notes on the following: gestational age, birth weight, date of admission to NICU, predisposing factors for NEC, comorbidities, preoperative clinical status, NEC diagnosis details, age, weight and date of laparotomy, surgical details, histology, time to discharge or death and long term clinical status in survivors. Electronic histology and radiology reports were searched to confirm diagnosis of NEC and preoperative radiological findings. No cases were excluded.

Descriptive statistics (data reported as median [range]) were calculated using GraphPad InStat. Paediatric Index of Mortality 2 (PIM2) Scores were calculated using the following parameters: systolic blood pressure (mm Hg), papillary reaction to bright light, PaO_2 (mm Hg), base excess (mmol/L), and mechanical ventilation at any time during the first hour in the intensive care unit, type of admission and whether the diagnosis was high or low risk [12]. A Mann–Whitney U test was used to compare PIM2 scores between those who did and did not survive beyond 30-days of laparotomy on NICU. $p < 0.05$ was considered statistically significant.

1.2. Surgical criteria and technique

Surgical evaluation and decision to operate were undertaken by the consultant paediatric surgeon. Decision to undertake the laparotomy on NICU was made in liaison with the neonatal intensivist and anaesthetist. Indications included neonates on HFOV and overall clinical impression that the neonate was too unstable to be safely moved to the OT. Low-birth weight was not an independent indication for surgery on NICU. The laparotomy was undertaken at the bedside using the staff and equipment from theatre. The operative procedure was undertaken in the same manner as in the OT.

2. Results

During the 10-year study period, 221 infants with NEC (Bell Stage II or III) were referred for surgical evaluation. Of these, 182 (82%) underwent surgery for NEC, 15 (8%) required a laparotomy in the NICU (Fig. 1). Patient demographics are shown in Table 1.

Among the fifteen infants who required laparotomy for NEC in the NICU, 13 (87%) were preterm and 2 (13%) were term babies. Of the term babies, one had panhypoparathyroidism with hypothyroidism, hypoglycaemia, hyponatraemia and hypotension, and the other term baby was a twin with IUGR and a birth weight of 1.7 kg. These two term babies both died early following laparotomy. Comorbidities among the preterm babies included chronic lung disease of prematurity in 9 neonates, PDA in 6, and intraventricular haemorrhage (IVH) in 4 (Table 2). Ten (67%) infants had pneumatosis intestinalis (PI), 5 (33%) had pneumoperitoneum (PP) and 1 (7%) had portal venous gas (PVG). None of the infants had both PVG and PP (Table 3).

The mean time from NICU admission to laparotomy in the unit was 15-hours (median 12 [1–72] hours). Five (33%) neonates had a peritoneal drain inserted prior to laparotomy. At laparotomy, 5 (33%) neonates had NEC totalis, 4 (27%) neonates had multifocal disease, 6 (40%) had focal disease. Five (33%) had an open and close laparotomy for NEC totalis, 8 (53%) had a stoma with/without bowel resection and 2 (13%) had bowel resection and primary anastomosis.

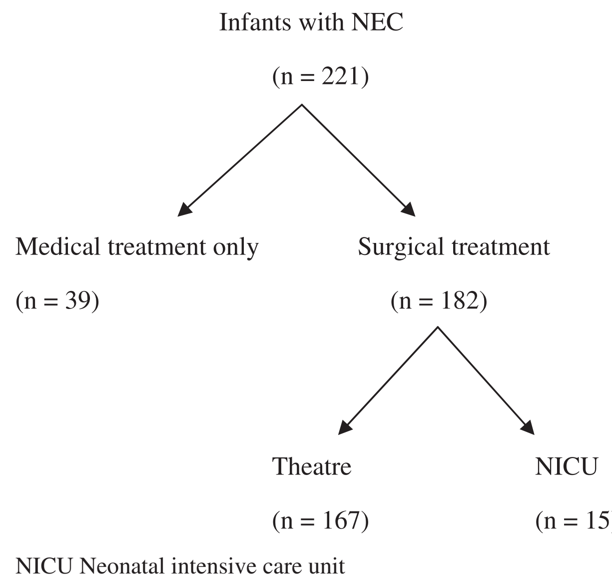

Fig. 1. Management of infants with NEC.

Five (33%) infants survived beyond 30 days of laparotomy. All required further surgery during their admission. One infant had a second laparotomy following a complication of enterocutaneous fistula; another had a relook laparotomy with further bowel resection, clip and drop and an abdominal patch application a day after primary laparotomy. Three infants underwent surgery for stoma closure; one infant had attempted closure of stoma at 4 weeks, however this was unsuccessful owing to persistent bleeding in the presence of dense adhesions whereas the other 2 infants had successful stoma closures.

Twelve of the 15 neonates died in total (80%). Ten (67%) died within 30 days of laparotomy, all of them within 72 hours of NICU admission. This is compared to a 32% (54/167) 30 day mortality in the NEC group who went to the OT at our institution during this time period. The median time from laparotomy to death in the NICU group was 6.5 hours (2–72 hours). Two of the 5 infants who survived beyond 30 days subsequently died; one died on PICU 8.4 months postprimary laparotomy following complications of SBS and sepsis-induced multiorgan failure and the other was discharged to their local hospital after 72 days and subsequently died from complications of SBS. Only 3 (20%) infants remain alive; one has mild developmental delay, the other two have no disability. The median follow up was 1.4 (0.5–7.5) years (Table 4).

Mortality following laparotomy on NICU was neither related to the type of procedure (stoma or anastomosis) nor time between admission to NICU and surgery. In relation to type of procedure, of the ten early deaths, 5 had open and close laparotomy for NEC totalis, 4 had formation of stoma for multifocal disease and only one had resection and anastomosis. Two of the five survivors who later died had multifocal disease, a stoma for one and anastomosis for the other. The remaining three who were long-term survivors all had a stoma for their initial laparotomy. Similarly, the median time from admission to NICU to surgery was 7 hours (range 1–72 hours) among those who

Table 1
Patient characteristics (n = 15).

Female gender, n (%)	8 (53%)
Gender, M:F	7:8
Birth weight, median (range)	1.06 (0.55–3.43) kg
Birth gestational age, median (range)	28.1 (23.7–40.0) wk
Weight at laparotomy, median (range)	1.45 (0.55–3.40) kg
Age at laparotomy, median (range)	21 (1–73) days
Corrected gestational age at laparotomy, median (range)	33.3 (23.9–42.1) wk

Table 2
Comorbidities (n = 15).

Comorbidity	n (%)
Chronic lung disease of prematurity*	9 (60)
Patent ductus arteriosus (PDA)	6 (40)
Medical treatment	1
Surgical treatment	1
No treatment	4
Intraventricular haemorrhage (IVH)†	4 (27)
Papille classification	
Grade 1	2
Grade 2	1
Unknown	1

* Three patients—not documented.
† Two cases no cranial ultrasound.

died (n = 12) and 24 hours (range 5–24 hours) among long-term survivors.

The mean Paediatric Index of Mortality (PIM2) Scores were 0.21 in the ten who died within 30-days of laparotomy and 0.17 in the five who initially survived ($p = 0.55$) (Fig. 2).

3. Discussion

Recent advances in neonatal care have led to a higher proportion of extremely low birth weight premature neonates surviving, increasing the population of neonates 'at risk'/predisposed to developing NEC [13,14]. Despite these advances in neonatal care, overall mortality rate has not decreased significantly, with reported rates of 30–50% for those neonates with NEC requiring surgery [15]. Infants with fulminant NEC requiring surgery pose a challenge to the paediatric surgeon, sometimes having no safe window to allow safe transfer to theatre for surgery, especially if requiring cardiorespiratory system support [4]. Traditionally, peritoneal drainage (PD) undertaken within the NICU setting was deemed useful in unstable neonates to decompress the abdominal compartment and hence allow improvement in their cardiorespiratory status [16]. However, a randomised controlled trial showed no survival benefit compared with primary laparotomy [17]. Hence, the authors concluded that PD is ineffective as either a temporising measure or definitive treatment and state laparotomy should be the first line surgical intervention [15].

Proponents of undertaking laparotomy for NEC on NICU argue that an unstable, critically ill neonate is exposed to significant physical and physiological risks associated with transfer to the OT [5,18]. Such risks include but are not limited to: manipulation and changing of equipment for transfer, exposure to changing temperature environments/risk of hypothermia, risk of dislodging vital tubes or clinical deterioration en route with inadequate staff and equipment to manage such difficulties, and sometimes delay in getting theatre space.

Our unit has no dedicated theatre suite in NICU and all these laparotomies were carried out by the bedside. This posed a challenge to the operating surgeon at times mainly from poor lighting and ergonometric constraints such as accessibility to the patient. The other constraints associated with operating on NICU include lack of a full armamentarium of surgical equipment when faced with unexpected and demanding/challenging circumstances. One neonate in this study had excessive bleeding which precluded full assessment of extent of disease. It is debatable if a more thorough assessment would have been possible if this was in the theatre environment. It has been argued that surgery on NICU increases the risk of infection [19–21], however recent studies have shown no such association [6–8,18,22].

Our study provides outcome data on both the mortality and long-term morbidity of critically ill neonates undergoing laparotomy for NEC on NICU. Consistent with previous studies comparing operative location, there was a higher 30-day mortality rate amongst the neonates operated on NICU (10/15; 67%) than the OT (54/167; 32%) ($p = 0.01$) [5–8,13]. This correlates with the unstable/critically ill nature of this patient population.

It is important to note that patterns of referral and clinical decisions pertaining to the provision of treatment will have an impact on NEC outcomes following treatment. At our institution, a tertiary hospital solely for children, the majority of neonates with NEC are transferred in from other centres for surgical evaluation resulting in a higher proportion of neonates with NEC requiring surgical intervention; 82% of neonates with NEC required surgery in this study compared to 20–40% quoted in the literature [23–26]. Inevitably with a higher proportion of neonates requiring surgical intervention, this population is likely to be sicker and hence has higher mortality rates than other institutions with a higher proportion of medically managed NEC where mortality rates are commonly quoted as 15–30% [23,25–30].

Institutions have different policies regarding criteria for operating on NICU. At our institution we only operate on neonates with NEC on

Table 3
Preoperative clinical status (n = 15).

	n (%)
Symptoms	
Abdominal distension	15 (100)
Bilious vomit/aspirate(s)	7 (47)
Blood in stool	2 (13)
Radiology	
Pneumatosis	10 (67)
Portal venous gas	1 (7)
Pneumoperitoneum	5 (33)
Laboratory	
DIC†	11 (73)
Glucose instability	6 (40)
Acidosis	13 (87)
Sepsis	15 (100)
Cardiorespiratory support	
Ventilated	15 (100)
HFOV	12
Conventional	3
Inotropes	15 (100)
One	2
Two	8
Three	4

† Disseminated intravascular coagulation.

Table 4
Clinical status of long-term survivors (n = 3).

Patient	Age at follow-up (years)	Morbidity
1	0.4	None
2	1.4	Mild developmental delay
3	7.5	None

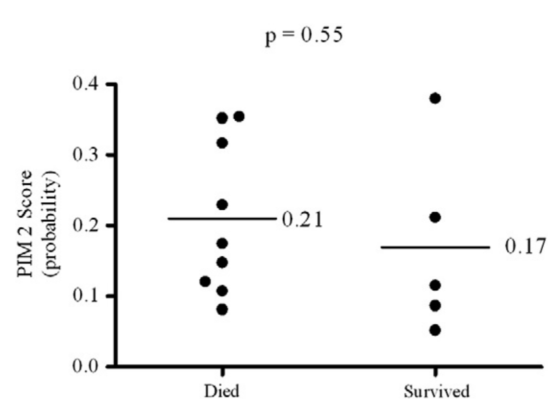

Fig. 2. Mean Paediatric Index of Mortality (PIM2) Scores in neonates undergoing laparotomy for NEC on NICU.

NICU who are deemed too critically ill/unstable to be safely transferred to the OT. Other institutions have a much lower threshold for operating on NICU, such as Frawley et al. who operate on all neonates with NEC < 1500 g in the NICU, and have a mortality rate of 33%, and Hall et al. who routinely operate on all neonates who are intubated and ventilated in the NICU [5,18]. Frawley et al. noted a higher mortality rate of 50% amongst neonates operated on NICU for NEC in earlier years when they had a much higher threshold for operating on NICU [5]. At our institution there is a policy to offer surgery to all neonates with NEC regardless of how critically ill or unstable they are, with the argument that even if there is only a small chance of survival with a good quality of life then surgical intervention should be undertaken. Inevitably this results in a higher mortality rate than other institutions that may utilise selection criteria to decide on the individual appropriateness of surgical intervention in these neonates.

Despite the critical condition of the neonates in this study, 20% (3/15) did survive long-term with minimal or no disability. This study gives some justification to our policy to continue to offer surgery to all infants with NEC regardless of how critically ill or unstable they are. However, this equates to five neonates having to undergo a laparotomy in order to achieve just one survivor. Our study has shown that 67% of these neonates died within a median of just 6.5-hours postoperatively. A further two (13%) underwent prolonged hospital stays related to multiple comorbidities and then later died after a number of months in hospital. We already know from previous evidence that the risk of neurodevelopmental delay in neonates with NEC is 45%, significantly higher than those with prematurity alone, and that this risk is 2.3 times higher in those requiring surgical intervention for NEC [31].

Hence, it is pertinent to ask—is surgery always in the best interests of the individual neonate? We must consider the impact that it has on their families; both those of neonates who die very soon after a laparotomy and those who suffer months/years with their child in hospital followed by an early death or lifelong disability.

Our study provides information about the outcomes in this patient population, which can be utilised by paediatric surgeons and neonatologists when counselling parents and making extremely difficult decisions regarding the care of these sick neonates. Similar to the importance of having an understanding of the risks of mortality and long-term morbidity amongst neonates born at 23-weeks when deciding on intervention, these outcome data allow parents and professionals caring for these sick neonates with NEC to make more of an informed decision regarding whether or not to undertake surgical intervention. The outcomes for these two populations are similar with neonates born at 23-weeks having a mortality rate of 81% and risk of neurodevelopmental impairment of 45% [32,33]. Hence, it seems appropriate to make an informed decision regarding surgical intervention for these sick neonates with NEC, based on a combination of current evidence, the clinical condition of the neonate, clinical judgement and parental wishes, rather than routinely operating on all.

Unfortunately, the PIM2 severity scoring system was unable to help distinguish those at highest risk of mortality from those more likely to survive. The PIM2 severity scores utilised in this study were calculated retrospectively, with inevitable inaccuracy related to the quality of the documentation. However, from 2008 Sequential Organ Failure Assessment (SOFA) severity scores have been calculated prospectively on all neonates at our institution, which may be utilised in the future for further research into this area. Multivariate models have been shown to be able to predict mortality risk with reasonable accuracy in other patient populations, such as the online ‘outcome estimator’ used to predict mortality in preterm infants, between 22 and 25 weeks gestation, in Australia [34,35].

Development of a prediction model for long-term morbidity and mortality for critically ill/unstable neonates with NEC requiring surgical intervention would be invaluable towards helping to make very difficult decisions regarding the management of these neonates on an individualised basis.

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