Surgical Necrotizing Enterocolitis - Association between surgical indication, timing and outcomes

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Abbreviations: Necrotizing Enterocolitis (NEC); Parenteral Nutrition (PN); British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS); Spontaneous Intestinal Perforation (SIP); Neonatal Intensive Care Unit (NICU); Patent Ductus Arteriosus (PDA).

Abstract

Background/Purpose

Despite improvements in neonatal care the outcomes of Necrotising Enterocolitis (NEC) remain unchanged over previous decades. The study aims to explore whether different indications for surgical intervention in NEC are associated with timing of surgery and outcomes.

Methods

Population-based, prospective, observational study of all 27 paediatric surgical centres in the United Kingdom and Ireland identified using the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System from 1st February 2013 to 28th February 2014. Infants were included if they had NEC and underwent first surgical intervention within 7 days of diagnosis. Primary outcomes were death, parenteral nutrition requirement or a composite outcome of death or PN requirement at 28 days post surgery.

Results

There were 133 infants meeting inclusion criteria. Indications for surgery were bowel perforation (n=67), suspected necrotic bowel without bowel perforation and not deemed to have failed medical management (n=20), those who had failed medical management (n=42) and a palpable mass without any other indication (n=4). Failed medical treatment as an indication for surgery was associated with an increased time to surgery of 30.28 (95% CI 13.46-47.10) hours from those whose indication was perforation and was also the strongest predictor of PN requirement or death at 28 days post-surgery (OR 4.54 [1.59-13.0]).

Conclusions

Failed medical treatment as an indication for surgery for NEC is associated with poor outcome. Earlier intervention in these infants represents a potential opportunity to improve outcomes in this population.

Level of evidence

Level I prognosis study

Key words

Necrotizing Enterocolitis, neonatology, surgical decision making

1 Introduction

Approximately a quarter of neonates with necrotizing enterocolitis (NEC) undergo surgical intervention usually in the form of laparotomy.[1] Following surgery, outcomes for NEC are often poor and of note are unchanged in recent years despite improvements in many other outcomes of neonatal care. Mortality following surgery from NEC remains as high as 50%.[2] In survivors there is a high prevalence of intestinal failure requiring long term parenteral nutrition and emerging evidence suggests that neurodevelopmental outcomes are unfavourable in these children.[2-4] In addition to those infants that undergo surgical intervention 20% of infants die of NEC prior to surgery.[5]

Indications for surgical intervention in NEC beyond perforation are an area of ongoing debate but surgical decision making has been highlighted as an area that has the potential to improve outcomes.[6] A survey of practice in the United Kingdom of consultant paediatric surgeons found a lack of agreement in the absolute and relative indications for surgical intervention. Seventy-five percent of respondents considered pneumoperitoneum an absolute indication for laparotomy, 71% of respondents considered failure of medical therapy to be an absolute indication and there was even less agreement on features such as abdominal mass on palpation or a fixed loop on abdominal radiograph.[7] It is unclear whether this uncertainty around need for, and timing of, surgery in infants with NEC has an influence on outcomes and there are few data examining this potential association. We therefore investigated the association between indication for surgery, timing of surgery and outcomes in infants undergoing laparotomy for NEC in a prospectively collected dataset.

1.1 Aims

1. To explore whether clinical features that prompt surgical intervention (indication for surgery) are associated with time from presentation to first surgical intervention for acute NEC.
2. To determine whether indication for surgery for acute NEC is associated with outcome.

2 Methods

2.1 Case definition and identification

Infants with NEC deemed to require surgery at any of the 27 paediatric surgical centres in the United Kingdom and Ireland were identified during a prospective cohort study using the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS) between 1st February 2013 to 28th February 2014.

Data collection took place as previously reported; in summary case identification was followed by mailing of a patient specific data collection form at both 28 days and 1 year following initial surgical intervention.[1] The case report forms collected data on demographic and clinical details, indication for and timing of surgery, surgical findings, procedures performed and outcomes.

Data for this secondary data analysis was obtained via application to the BAPS-CASS committee with provision of a formalised analysis plan. Ethical approval for the collection of the dataset was from the National Research Ethics Service (NRES) South Central- Oxford A committee (ref: 12/SC/0416). No further permissions were required for secondary analysis of this anonymised dataset.

2.2 Inclusion and exclusion criteria

Only babies with a decision to undergo surgical intervention for NEC were included in the dataset and cases were only included if they had confirmed NEC at laparotomy or post mortem. Therefore cases of SIP were excluded. In order to focus on acute surgical intervention for NEC, infants in whom surgery took place over 7 days from disease onset were excluded. Since this dataset was from an epidemiological study of all surgical interventions for NEC, it included a number of infants who had surgery for later complications of NEC including persistent intestinal obstruction or stricture. To limit included cases to those who underwent surgery during the acute phase of their disease we excluded infants with a duration from first suspicion of NEC to initial surgical intervention of more than 7 days.

2.3 Indications for surgery

Indications to undertake surgery were recorded by the operating surgeon and therefore reflect the decision making process at the time of decision to undergo surgery. As an observational study of current practice these were determined by the clinician rather than associated with a set definition. Hierarchical clustering was used to place infants in discrete groups based on indication for surgery as reported by the operating surgeon.

2.4 Outcomes

Primary outcomes of interest were death within the first 28 days of initial surgical intervention, PN requirement at 28 days following first surgical intervention in survivors, and a composite of these two outcomes. PN requirement at 28 days was used specifically as it was shown to be a predictor of 1 year mortality after adjustment for confounding variables reported in this dataset previously.[8] Secondary outcomes included duration of PN required, length of inpatient stay and mortality rate at 1 year following initial surgical intervention.

2.5 Statistical analysis

Data were analysed as specified in the secondary analysis protocol. Statistical analysis took place using StataSE v15 (StataCorp LLC, Texas, USA). Characteristics of infants, including gestational age, birthweight and markers of disease severity, such as need for inotropes, were described. Time from diagnosis of NEC to surgical intervention was derived from case report forms and is presented as hours. If an infant underwent peritoneal drainage as the first surgical procedure then the time of this was used as timing of first surgical intervention, even if subsequently followed by laparotomy. Data are presented as median (range) and percentages are rounded to 1 significant figure.

Fisher's exact test or chi-squared test, as appropriate, were used for comparison of categorical data and the Mann Whitney-U test or Kruskal-Wallis test was used for non-parametric continuous data with two or more than two categories respectively. Multivariable linear or logistic regression was used to explore associations between variables of interest and outcomes taking into account clinically important and meaningful confounders. The selected variables for the multivariable models were those which reached statistical significance in the univariate analysis of factors associated with poor outcome or which were

significantly associated with indication for surgery. A P value of less than 0.05 was considered as statistically significant. Hierarchical clustering was used to group infants based on presenting features and indication for surgery as defined in the case report form in order to direct analyses.

3. Results

3.1 Cases and presentation

There were 189 infants included in the observational cohort. Those in whom the indication for surgery was a NEC related intestinal stricture (n=13) or those in whom the time from to first surgical intervention was more than 7 days (n=43) were excluded.

The remaining 133 infants with a median gestation at birth of 27 (22-41) weeks and birthweight of 950 (460-4140) grams were all included. The median age at presentation was 11 (1-104) days. Ninety nine (74%) of these infants were transferred to a neonatal surgical centre for treatment following the diagnosis of NEC. Infants not requiring transfer and therefore already receiving care at a neonatal surgical centre at the time of diagnosis had a lower gestational age at birth (25 [23-40] *vs* 27 [22-41], p=0.02) and were more likely to have a patent ductus arteriosus (PDA) (25 [74%] *vs* 50 [51%], p=0.03) compared to those transferred in. At presentation of NEC, 35 (26%) infants were receiving inotropes and this increased to 56 (42%) neonates at the time of surgical intervention.

3.2 Indication for surgery

Indications for surgery were bowel perforation (n=67), suspected necrotic bowel without bowel perforation and not deemed to have failed medical management (n=20), those who had failed medical management (n=42) and a palpable mass without any other indication (n=4). These indications were as recorded from the operating surgeon. For the purpose of analysis the 4 infants in whom a palpable mass was the indication for surgery were excluded from sub-group analyses due to small group size. Clinical and surgical details of these groups are shown in Table 1.

3.3 Time to first surgical intervention

The median duration of time from first suspicion of NEC to first surgical intervention, was 36 (0.7-168) hours. Time from presentation to surgical intervention was similar for infants who were already at a neonatal surgical unit and those who were transferred in (36 [2-168] *vs* 36 [0.7-159] hours, p=0.65). However, the time from presentation to surgical intervention differed depending on the indication for surgery. Infants in whom the indication for surgery was failed medical treatment had a longer duration to surgery than those in whom the indication for surgery was perforation or who had suspected necrotic bowel (Table 1). Not shown in the table are those infants with a palpable abdominal mass (n=4) who underwent surgery 65 (26-96) hours following diagnosis. During this time the requirement for inotropic support increased in all three groups (Table 1) but only reached statistical significance in the infants in whom indication for surgery was failed medical treatment (p=0.02). On multivariable analysis, following adjustment for confounding factors, failed medical treatment remained the only factor that was significantly associated with duration to surgery (Table 2).

3.4 Surgical findings and interventions

The first surgical intervention carried out in each infant was bowel resection with stoma formation (n=70, 53%), stoma formation alone (n=22, 17%), bowel resection with primary anastomosis (n=14, 11%), peritoneal drain insertion (n=10, 7.5%), open and close laparotomy due to NEC totalis with palliation (n=7, 5.3%), bowel resection with 'clip and drop' (n=6, 4.5%) and laparotomy with no intervention (n=4, 3%). Peritoneal drain insertion was used more frequently in neonates with a perforation (table 1) and in those with a perforation requiring inotropes at NEC presentation compared to those without inotropes (7 [32%] *vs* 2 [4.4%], p=0.007). All those who initially underwent peritoneal drain insertion (n=10) went on to have a laparotomy that involved bowel resection and stoma formation (n=4), stoma formation alone (n=3), bowel resection with primary anastomosis (n=2) or bowel resection with 'clip and drop' (n=1).

Necrotic bowel requiring resection (or palliation in 7 infants due to panintestinal necrosis) was found in 104 (78%) infants overall and in 53 (79%) of those with a perforation, 15 (75%) of those with suspected necrotic gut, 33 (79%) infants with failed medical management and 3 (75%) infants with a palpable mass.

3.5 Outcomes

There were 30 (23%) deaths within 28 days of operative intervention and 36 (32%) within 1 year. Of those who survived to 28 days, 41 (40%) remained on PN with a median of 36 (3-287) days of PN following surgery. The median length of stay was 91 (17-381) days post-surgery. In univariable analyses, the only feature significantly associated with death at 28 days was need for inotropes at time of presentation, whereas younger gestational age at birth and indication for surgery were both associated with PN requirement at 28 days (Table 3). For the composite outcome of either death or PN requirement at 28 days post-surgical intervention there was a significant association with younger gestation at birth, inotropes at presentation of NEC and not undergoing transfer from another NICU (note higher incidence of poor outcome if no transfer required). Total days of PN post op (19.5 [3-382] *vs* 57 [12-387] *vs* 57 [8-381] days, p=0.08), post-operative length of stay (119 [17-381] *vs* 98 [27-192] *vs* 83 [30-231] days, p=0.31) and 1 year mortality (17 [32%] *vs* 9 [45%] *vs* 10 [27%], p=0.38 were similar between the 3 groups in univariable analyses based on indication for surgery, although there was a trend towards shorter duration of PN required in infants in whom the indication for surgery was perforation.

On multivariable logistic regression analysis lower gestational age at birth, not undergoing transfer from another NICU, requiring inotropes at presentation and an indication for surgery of suspected necrotic bowel or failed medical treatment were all associated with increased 28 day mortality or PN requirement (table 4). Factors associated with each component of this composite outcome are shown in tables S1 and S2 (Appendix).

4. Discussion

In this large population based study of infants deemed to require surgical intervention for acute NEC, we have identified an association between the indication for surgery and outcome. Furthermore we have identified an association between indication for surgery and the time between initial suspicion of NEC and surgery, Of particular concern is the group of infants who undergo surgery for ‘failed medical

treatment'; these infants have the longest period of time between initial presentation with NEC and surgery, and also have the worst outcomes.

The strengths of this study are the use of an existing large, prospectively collected, population-based dataset and our ability to classify indication for surgery into distinct groups allowing an analysis that we believe is novel. In our analysis we have adjusted for other factors that may influence timing of surgery and outcome including gestational age, age, requirement for inotropes and need for transfer to a surgical centre. The principal weakness of this study is that the data are observational so we are only able to report associations rather than infer causation. Additionally, as an observational study some variables were not specifically defined including the definitions of the indications for surgery nor what operative procedure should be performed. As such, further work is required to validate and interrogate the hypotheses we raise. However, this methodology has the benefit that we have captured real-life clinical practice of surgeons treating infants deemed to require surgery for NEC rather than practice that may be influenced by arbitrary definitions in a prospective study and thus may not reflect contemporary surgical practice. We also acknowledge that the outcomes assessed here are limited. We have focussed on important short term outcomes that have been shown in previous work to be associated with outcome at 1 year of age [8] and which we believe are relevant when considering the impact of surgical intervention on an acute condition. Nonetheless we recommend that any prospective analysis should record a wider range of outcomes including, importantly for this population, neurodevelopmental outcome which would require longer follow-up.[9] A final limitation is that as a UK based observational study we are unable to comment on whether these findings are applicable to other healthcare settings.

Whilst the principle of surgery for NEC is early intervention to reduce contamination and sepsis without subjecting infants with non-ischaemic bowel to unnecessary surgery [10, 11], the lack of agreement in indications of surgery amongst surgeons [7] suggest that these principles may be implemented with variation. As such the decision making process around the time of surgery represents a potential opportunity to influence outcome [12], something that is desperately needed for infants with NEC [2].

Our analysis suggests surgeons distinguish between infants with different presenting features and time their surgical intervention as they deem appropriate. Infants in whom the indication for surgery was

perforation or suspected necrotic bowel undergo surgery earlier than those in whom the indication was failed medical treatment. Given the difference in outcomes between these groups, the timing of surgery particularly in the failed medical treatment group represents a potential opportunity to improve outcome.

In similarity to previous studies [13, 14] the indication for surgery in this cohort was intestinal perforation in approximately half of all infants. These infants had the shortest duration of time to surgical intervention despite three quarters of them requiring transfer into a surgical unit. This reaffirms previous studies that suggest pneumoperitoneum is the most widely recognised as an absolute indication for surgery[7]; surgeons proceed to surgical intervention without delay. Whilst this indication for surgery is also associated with the best outcome (Table 4) it is unclear whether this is due to patient or disease factors, or that they received, in the main, prompt surgical intervention. Najaf et al identified that infants with NEC who develop a perforation typically do so early in their disease course.[13] It is possible that this is a particular subgroup of infants who are typically extremely preterm, have a relatively early onset of NEC (median 8 days in this study) and are more prone to perforation. Any of these factors in addition to prompt surgical intervention may confer an outcome advantage. (We emphasise here that we have taken all steps possible to exclude infants with SIP from this report altogether). It is also clear that peritoneal drainage is employed more frequently in this group of infants but the most commonly undertaken intervention, by far, was laparotomy (92%). The finding that this method is used more frequently for infants with a perforation represents a possible source of bias however when adjusting for this in the multivariable models there was no difference to the models and they were not strengthened by including this variable (data not shown).

Even in infants without intestinal perforation, suspicion of necrotic bowel as an indication for surgery was associated with a short time period from diagnosis to surgery. This suggests that surgeons are able to recognise infants whom they believe have necrotic bowel (even in the absence of perforation) and arrange surgery promptly. In fact median time to surgery was shortest in this group despite again 70% being transferred from another unit. Given there is no unifying way to categorically determine whether an infant has necrotic bowel or not, this suggests that surgeons are currently using their clinical

experience to make this judgement. Previous studies have explored ways of identifying infants with necrotic bowel using a variety of biomarkers including interleukins[15-17], intestinal fatty acid binding protein[18, 19], novel urine peptides[20], serum amyloid A[21], platelets[21] and heart rate characteristics[22] along with combinations of these in the form of a scoring system[23, 24]. Each of these methods has its limitations and none have been adapted into widespread practice. In infants in whom suspected necrotic bowel was the indication for surgery, outcomes were worse than those undergoing surgery for perforation, despite similar patient demographics and time to surgery. We postulate that these infants were more systemically unwell (necrotic tissue is known to be a key driver of the systemic inflammatory response [25]) and that the worse outcome was therefore most likely a reflection of their disease status.

The third group of infants, comprising approximately one third of all infants who underwent surgery for NEC, were those in whom the indication for surgery was failed medical treatment. Whilst it is impossible from this study to identify precisely what failed medical treatment means to each individual surgeon, this is a well-recognised indication for surgery [7]. Unsurprisingly, time from diagnosis to surgery was longest in this group. Of note there is evidence of clinical deterioration between diagnosis and surgery for this group with inotropes being required in 19% at the time of diagnosis, rising to 45% by the time of surgery. Of concern is the association between this indication for surgery and the highest chance of poor outcome. Whilst the reason for this association cannot be ascertained from this study our analysis of time from diagnosis to surgery raises the possibility that earlier surgery in this group may improve outcome. As with all groups, approximately 70% of infants in this group were actually found to have necrotic bowel at laparotomy. Given this group have the longest time to surgery and the worst outcomes it is possible that earlier surgery may have been beneficial. In order to explore this hypothesis further it is essential to be able to identify infants that may benefit from surgery earlier than is currently possible to allow a comparison to take place. Any move to intervene with surgery earlier in the disease course of NEC should be accompanied by monitoring for cases in which necrosis has not yet developed to ensure timing is optimal and unnecessary intestinal resection does not occur.

An interesting and unexpected observation is that the composite poor outcome of mortality or PN dependence at 28 days was higher in infants that were already at a surgical centre compared to those transferred in. Possible explanations for this include that infants at a surgical centre had a younger gestation at birth and increased incidence of PDA. It is also possible that this higher mortality at surgical centres is skewed by a number of infants at non-surgical centres being considered to be too unwell for transfer and dying without surgical assessment, or that sicker infants were transferred in to surgical centres *in utero*. A previous population based report of NEC in a time period similar to this study but using a different method of data collection, identified that 20% of all infants who died from NEC did so prior to transfer to a surgical centre. The dataset we have used only included infants who were assessed at a surgical centre. [26]

5. Conclusion

This study suggests that surgeons make decisions regarding the timing of surgical intervention in infants with NEC based on their clinical assessment. Infants with intestinal perforation or in whom there is suspicion of necrotic bowel undergo prompt surgical intervention. The remaining third of infants who do eventually undergo surgery do not display clinical or radiological signs sufficient enough to convince a surgeon that surgery is justified or necessary at initial assessment. Infants in this group have the worst outcomes with more than four times the odds of death or PN requirement at 28 days compared to infants who undergo surgery due to a perforation. Earlier surgery in this group of infants therefore represents a potential opportunity to improve outcome. We recommend that research efforts focus not only on prevention of NEC but on methods to assist surgeons in identifying earlier those infants with disease that will ultimately require surgical treatment.

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Table 1. Group characteristics based on indication for surgery					
		1:Perforated (n=67)	**2: Suspected Necrotic bowel (n=20)**	**3: Failed medical treatment (n=42)**	**P**
Gestation at birth (weeks)		26 (22-40)	28 (24-41)	27 (23-39)	0.16
Birthweight (g)		930 (530-3580)	1155 (590-3900)	903 (460-4140)	0.31
Age at presentation (days)		8 (1-56)	8 (1-93)	28 (2-104)	**0.0001**
Corrected gestational age at presentation (weeks)		28.6 (23.4-43)	32.3 (24.3-48.7)	31.7 (25.4-49)	**0.0007**
PDA		36 (54)	7 (35)	30 (71)	**0.02**
Other anomaly (non cardiac)		8 (12)	4 (20)	7 (17)	0.61
Ventilated at presentation		42 (63)	11 (55)	24 (57)	0.76
Ventilated at surgery		60 (90)	18 (90)	36 (88)	0.95
Inotropes at presentation		22 (33)	6 (30)	8 (19)	0.29
Inotropes at surgery		27 (40)	9 (47)	19 (45)	0.81
Abdominal wall discoloration at presentation		15 (22)	5 (25)	9 (21)	0.95
Abdominal wall discoloration at surgery		18 (27)	10 (50)	16 (38)	0.13
Transferred from other NICU		52 (78)	14 (70)	31 (74)	0.76
Time from presentation to operation (hrs)		23.5 (2-167.5)	18.8 (0.7-79)	69.3 (5-159)	**0.0001**
Operation performed	**Laparotomy no intervention**	1 (1.5)	1 (5.0)	2 (4.8)	**0.007**
	Resection with anastomosis	5 (7.5)	0 (0)	8 (19)	
	Stoma with resection	38 (57)	8 (40)	22 (52)	
	Stoma no resection	10 (15)	4 (20)	7 (17)	
	Clip and drop with resection	1 (1.5)	4 (20)	1 (2.4)	
	Open and close (NEC totalis)	3 (4.4)	2 (10)	2 (4.8)	
	Peritoneal drain	9 (13)	1 (5)	0 (0)	

Table 1. Group characteristics based on indication for surgery. PDA = patent ductus arteriosus. NICU = neonatal intensive care unit. Figures are median (range) or n (%).

Table 2. Factors associated with duration of time in hours from presentation of NEC to first surgical intervention.		
	Hours difference (95% CI)	**P**
Increase in gestation at birth per week	-0.45 (-2.06 to +1.15)	0.58
Increase in age at presentation per day	-0.22 (-0.60 to +0.16)	0.26
Inotropes at presentation	-1.58 (17.47 to +14.31)	0.84
Transferred from other NICU	+1.84 (-14.58 to +18.26)	0.83
Indication for surgery		
Perforation	reference	-
Suspected Necrotic Bowel	-11.49 (-32.72 to +9.74)	0.29
Failed medical treatment	+30.28 (13.46 to +47.10)	**0.001**

Table 2 - Multivariable linear regression analysis of factors associated with duration of time in hours from presentation of NEC to first surgical intervention. For indication for surgery, the reference group is bowel perforation. The hours difference is adjusted for all other variables included in the table. CI = confidence interval. NICU = neonatal intensive care unit.

Table 3. Factors associated with poor outcome									
	PN day 28 post surgery[$]			**Deceased day 28 post surgery**			**PN or deceased day 28 post surgery**		
	Yes (39)	**No (60)**	**P**	**Yes (30)**	**No (99)**	**P**	**Yes (69)**	**No (60)**	**P**
Gestation at birth (weeks)	26 (23-39)	28 (23-41)	**0.002**	26 (22-38)	27 (23-41)	0.20	26 (22-39)	28 (23-41)	**0.001**
Age at presentation (days)	16 (1-93)	10 (1-104)	0.11	9 (1-75)	11 (1-104)	0.40	11 (1-93)	10 (1-104)	0.35
Inotropes at presentation	14 (36)	11 (18)	0.06	10 (33)	25 (25)	0.48	24 (35)	11 (18)	**0.047**
Transferred from other NICU	27 (69)	51 (85)	0.08	19 (63)	78 (79)	0.10	46 (67)	51 (85)	**0.02**
Time from presentation to operation (hrs)	38 (2.8-159)	38 (0.7-168)	0.64	24 (2.3-138)	38 (0.7-168)	0.12	34 (2.3-159)	38 (0.7-168)	0.39
Indication: Perforation	14 (25)	37 (75)	**0.03**	16 (24)	51 (76)	0.63	30 (45)	37 (55)	0.11
Indication: Suspected Necrotic Bowel	6 (43)	8 (57)		6 (30)	14 (70)		12 (60)	8 (40)	
Indication: Failed medical treatment	19 (56)	15 (44)		8 (19)	34 (81)		27 (64)	15 (36)	

Table 3. Factors associated with poor outcome. $ = only including survivors. Figures are median (range) or n (%).

Table 4. Multivariable logistic regression analysis of factors associated with PN requirement or death at 28 days post surgery.		
	Adjusted odds ratio (95% CI)	**P**
Increase in gestation at birth per week	0.85 (0.77-0.94)	**0.001**
Increase in age at presentation per day	0.99 (0.97-1.01)	0.26
Inotropes at presentation	3.25 (1.28-8.26)	**0.01**
Transferred from other NICU	0.34 (0.13-0.88)	**0.03**
Increase in time from presentation to operation per hour	0.99 (0.98-1.00)	0.17
Indication for surgery		
Perforation	reference	-
Suspected Necrotic Bowel	3.85 (1.04-14.3)	**0.04**
Failed medical treatment	4.54 (1.59-13.0)	**0.005**

Table 4 - Multivariable logistic regression analysis of factors associated with PN requirement or death at 28 days post surgery. For indication or surgery, the reference group is bowel perforation. The odds ratio is adjusted for all other variables included in the table. CI= confidence interval. PN= parenteral nutrition.