World Journal of Surgery and Surgical Research

Research Article
Published: 07 Aug, 2023

Laparotomy or Peritoneal Drainage - A Surgeon's Dilemma in the Treatment of Necrotizing Enterocolitis in Low Body Weight Neonates

*Dionysis TN**

Department of Pediatric Surgery, Athens Children's Hospital 'Pan & Aglaia Kyriakou', Greece

Introduction

Necrotizing Enterocolitis is an acute inflammatory disease of the intestine causing damage to the mucosa, necrosis and perforation. It is the most common gastrointestinal surgical emergency, occurring in low birth weight and premature neonates weighting less than 1,500 g and it is associated with increased mortality (50%) and comorbidities [1]. Surgical intervention remains the cornerstone for the treatment of NEC in LBW neonates. However, controversy exists on the best, safest, most efficient and less invasive (less painful) approach in the management of this devastating disease. A variety of surgical techniques have been documented including resection and anastomosis, enterostomy, peritoneal drainage and laparotomy, albeit without consensus [2,3].

A meta-analysis of ten retrospective studies was conducted by Moss et al. [4] aiming at determining which surgical intervention, PD or LAP is the most effective in premature neonates with NEC or intestinal perforation. According to the authors due to treatment bias, it was not possible to determine whether PD or LAP was superior, improving survival. To date, two RCTs have been undertaken analyzing the impact of PD and LAP in perforated NEC [5,6].

Given the high mortality and morbidities of NEC in neonates, there is need to identify surgical interventions that can be used in the treatment and more importantly to reduce mortality in patients.

The purpose of this systematic review is to conduct an up-to-date literature search and to compare evidence on the effectiveness of laparotomy and peritoneal drainage on the survival of LBW and premature neonates with NEC.

Methods

This review was carried out using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines as a methodological template [7] (Supplement Table 1). The research question to be addressed was "Does laparotomy or peritoneal drainage affects survival in neonates with NEC"?

Literature search strategy

We applied a comprehensive literature search of publications up to December 2016 using the following seven databases: Mendeley, Cochrane Central Register of Controlled Trials, PubMed, CINAHL (EBSCO), Medline, Embase, Scopus and extended back to 1946. In an effort to capture all published studies from a variety of international journals no restrictions were applied on language, age or publication dates. Also, supplementary studies were sought from conference proceedings as well as two clinical trials registries, Australia and New Zealand (ANZCTR) and International (clinicaltrials.gov). Other potentially relevant citations were identified by hand search of the reference lists of relevant articles, reviews, systematic reviews and meta-analyses.

The database search was conducted using a two-step search strategy as follows:

Search 1: "necrotizing enterocolitis AND surgery AND neonates AND premature"

Search 2: "necrotizing enterocolitis AND surgery AND neonates"

Search 3, was a combination of both searches using the term "OR" (Supplement Table 1).

Study eligibility criteria

Type of studies: This meta-analysis considered all types of study designs including Randomized

OPEN ACCESS

***Correspondence:**

Theodoros-Nektarios Dionysis, Department of Pediatric Surgery, Athens Children's Hospital 'Pan & Aglaia Kyriakou', Athens, Greece, Tel: (0030)2132009169

Received Date: *11 Jul 2023*
Accepted Date*: 02 Aug 2023*
Published Date*: 07 Aug 2023*

Citation:

Dionysis TN. Laparotomy or Peritoneal Drainage - A Surgeon's Dilemma in the Treatment of Necrotizing Enterocolitis in Low Body Weight Neonates. World J Surg Surgical Res. 2023; 6: 1488.

Controlled Trials (RCTs), non-randomized controlled trials, intervention studies, cohort, case-series, prospective and retrospective studies.

Outcome measures: Primary outcomes considered were survival or mortality rate.

Selection criteria: Selection criteria were based on Population, Intervention, Comparator and Outcome (PICO) characteristics [8]. The population of interest was 'low birth weight neonates or premature infants with NEC', 'Laparotomy or peritoneal drainage' were the interventions and 'survival or 'mortality' were the outcomes.

Exclusion criteria: Publications were not included for the following reasons: Reviews, systematic reviews, editorials, comments, letters, newspapers, as well as those with no abstract, no full-text or no English translation. Interventions other than surgery such as enteral/parental feeds, vitamin supplementation, probiotics, oral immunoglobulin, were considered to be irrelevant. Also deemed inappropriate were studies focusing on microflora, antibiotic therapies, cardiac function, acute appendicitis pain control, neurodevelopment, intestinal atresia, bowel/intestinal stenosis, short bowel syndrome, spontaneous intestinal perforation, pneumatosis intestinalis, intussusception, preeclampsia, colonic stenosis, congenital malformations, gastroschisis, delayed cord clamping, respiratory function, liver dysfunction, patent ductus arteriosus, hemodynamic, small bowel perforation, ileostomy, colonic strictures, Hirschsprung's associated enterocolitis, bowel necrosis, cytokine and gene expression correlation in NEC and diagnostic tests (radiology, histology, sonography). Finally, studies focusing on a combination of PD and LAP were omitted.

Selection procedure of studies: Initially, all titles and abstracts of publications retrieved by the database search were screened against eligibility criteria by two investigators (TD and ET), after which duplicates were removed. Potentially eligible abstracts were selected for full-text reading. In the case, when there was insufficient information in the abstract to warrant exclusion of the article, the full-text was also retrieved. Both reviewers then independently appraised full-text papers for inclusion and details were extracted. Discrepancies were resolved by discussion and consensus that led to agreement. In addition, reference lists and bibliographies of relevant publications, systematic reviews, meta-analyses and reviews were cross-checked for supplementary material (Figure 1).

Quality assessment

Two independent reviewers (TD, ET) assessed relevant papers for methodological validity using critical appraisal instruments according to Joanna Briggs Institute (JBI) [9]. Three JBI checklists (RCT,

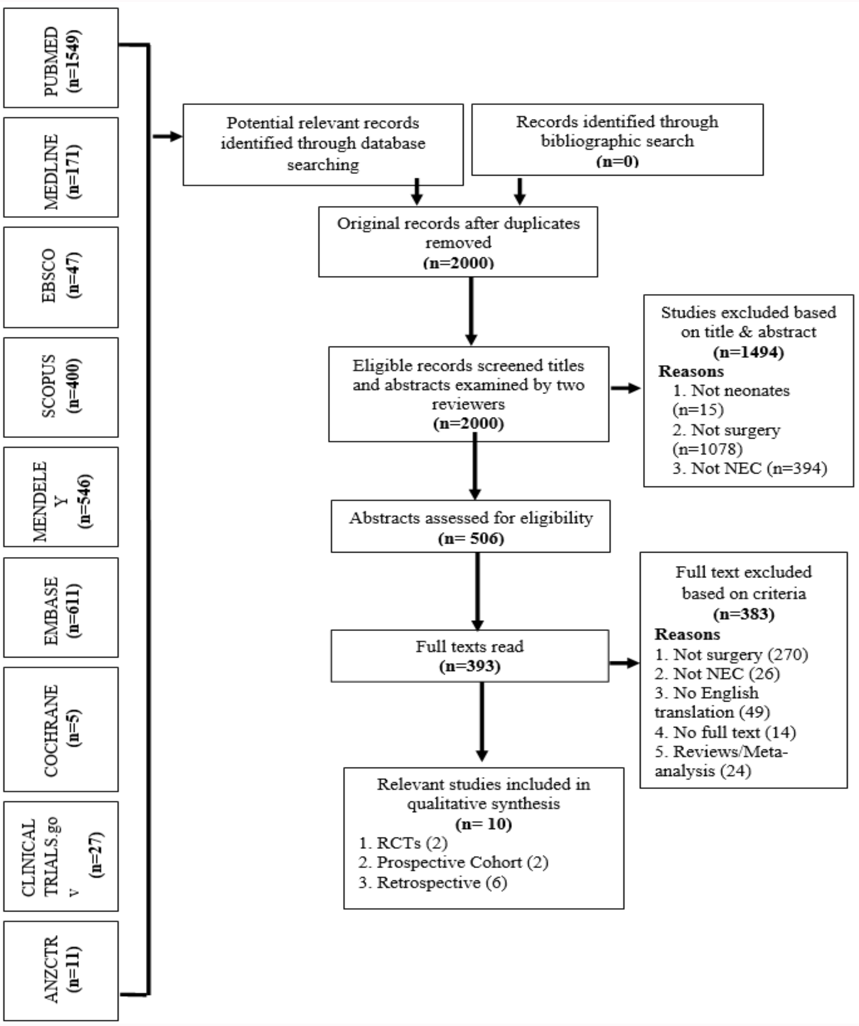

Figure 1: Flow chart of search details.

cohort, and case-series) based on study design were used to assess methodological quality of the included studies (Supplement Table 2). Retrospective reviews were appraised using the JBI case-series checklist. Each checklist consisted of 10 to 13 questions evaluating the validity, reliability, feasibility, appropriateness of statistical tests and clinical importance of study methodologies. Questions described the study design, target population, selection criteria, exposure and outcome measures, follow-up, the appropriateness of the statistical analysis, controlling of confounders and identifies potential bias that might have been omitted. Also, in the case of RCTs, whether patients were blinded and randomly allocated to treatment groups was examined. Three possible responses were available for each question, 'yes', 'no', 'unclear' or 'not applicable'. In order to quantify assessment of each study a score was given to each response. For a response of 'yes' a score of 1 was allocated and '0' for 'no' or 'not applicable'. The final result was the sum of the scores for each question. Scores higher than 50% were considered to be of good quality and below 50% poor quality [10]. Any disagreements that arose between the authors were resolved through discussion.

Data collection

Data extracted from relevant papers included details relating to: Authors, year of publication, study name, study design, geographic location, sample size, gestational age, birth weight exposure (laparotomy or peritoneal drainage), outcome measures, main findings which were tabulated and qualitatively synthesized (Table 1). Where available, data analysis results were reported as survival/ mortality rate. A meta-analysis of these studies was conducted producing a final conclusion to be used as a foundation for evidence-based practice.

Results

Electronic search

The literature search identified a total of 3,367 potential publications of which 2,000 remained, after removal of duplicates (Figure 1). No citations were found by cross-checking of reference lists. Two reviewers (TD, ET) independently screened the 2,000 potential papers by scanning titles and abstracts. A total of 1,494 were excluded based on no abstract (6), not the intervention surgery (1078), not in neonates (15) or the outcome necrotizing enterocolitis (394), leaving 506 eligible abstracts. Of the remaining 506 abstracts, 113 papers were excluded for the following reasons: No abstract (8), not surgery (84), not NEC (11), and no English translation (10), leaving 393 articles for full-text reading. A total of 383 full-texts were deemed to be inappropriate (270 not surgery, 26 not NEC, 49 no English translation, 14 no full-text available, 24 reviews and meta-analysis) leaving a total of 10 publications relevant to the topic for qualitative synthesis (Figure 1).

Study characteristics

The database search identified ten relevant studies (2 RCTs, 2 Prospective cohorts and 6 Retrospective) conducted from 1998 to 2014 [5,6,11-18] focusing on the effect of Lap or PD on survival and mortality of neonates with NEC (Table 1). Six Retrospective studies [11,13,15-18] examined chart reviews dating from 1953 to 2009. Six studies were performed in USA [5,12-16], two in Canada [5,11], one in Saudi Arabia [17] and Turkey [18] and one international study involving centers in Europe, UK and Australasia [6]. Diversity existed among study design regarding sample size, gestational age and weight distribution of the population. Sample size ranged from 25 to 188, 703. Overall, a total of 189,291 neonates were investigated with gestational age ranging from 18.4 to 36 weeks and birth weight less than 1,500 g. Only one study included patients with average body weight more than 1,500 g [18]. Neonates diagnosed with intestinal perforation or critically ill and of very LBW (<1000 g) were more likely to have initial PD, whereas those with NEC were operated using LAP. Two outcomes were assessed, mortality and survival rate. Regarding the outcome of surgical intervention (PD and LAP) in neonates, inconsistencies were reported among studies. Data analysis of 9 studies indicated higher mortality in patients subjected to primary PD as compared to LAP [5,6,11-17]. Five of the publications (2 RCTs, and 3 retrospective) reported no statistically significant results [5,6,13,16,17].

In most cases, when primary PD was the intervention of choice, patients deteriorated and a salvage LAP was required [11,13-15]. However, laparotomy alone or primary PD supplemented by laparotomy resulted in a lower mortality rate than with PD alone [14]. On the other hand, one study documented that PD alone was effective [18], although it was advised that laparotomy should be used in patients not responsive to PD. In this study, 25 neonates with mean gestational age of 32.08 ± 3.75 and mean birth weight >1500 g were allocated into two intervention groups (LAP *vs.* PD). Ten patients were assigned to the Laparotomy group and 15 to the PD group. In the Laparotomy group 2/10 (20%) neonates survived and 8/15 (53.3%) in the PD alone. However, LAP was performed in 4 patients from the PD group because of clinical deterioration, after which 3 survived. Summarizing the findings documented, although primary PD as compared to Laparotomy may be the less invasive intervention with regard to morbidity in LBW patients (<1000 gm), in the majority of cases, a salvage laparotomy will be required in patients. Overall, laparotomy as a surgical intervention in neonates with NEC resulted in higher survival rate (50%-86%) than in patients subjected to PD (11%-50%) (Table 1).

Quality assessment

Qualitative assessment of publication using JBI critical appraisal checklists revealed that the majority of studies (9/10) had scores above 50% threshold and can be rated as having 'high quality' (Tables 2A-2C). Only one study (1/10) (Nobel), had a 'poor' score (30%) below the threshold due to insufficient data regarding inclusion criteria, clinical information, follow-up, demographic information and statistical tests applied, thus, resulted in poor reliability, validity and clinical significance (Table 2A). Quality assessment results according to JBI Critical Appraisal List for RCTs (Table 2B). Quality assessment results according to JBI Critical Appraisal List for Cohort studies (Table 2C). Quality assessment results according to JBI Critical Appraisal List for Retrospective Chart reviews.

Meta-analysis

A meta-analysis was performed using Cochrane's Rev Man 5 software [19]. Ten studies were used to assess the research hypothesis whether PD or Laparotomy improves survival in neonates with NEC [5,6,11-18]. For the meta-analysis, 'mortality' outcome was used. The Chi square statistic (I^2) was used to determine the degree of heterogeneity among studies and p-value was considered to be significant at the 5% level (Figure 2) [20]. Publication bias was assessed using the funnel plot (Figure 3).

Figure 2 may represent moderate heterogeneity as indicated by the I^2 statistic (44%) being between 30% to 60% and a p-value >0.05 [20,21]. The overall effect (black diamond) is close to the line of null

Table 1: Characteristics of relevant studies in this systematic review.

Study/Date/Country	Study design	n	Gestational age	Birth weight	Group (n)/ Surgical technique (n)	Outcome assessed	Survival rate (%)	Mortality (%)	Findings
Moss et al. [1] 2006; (NECSTEPS) Multicentre USA & Canada	RCT	117	23.7-28.3 weeks	<1500 gm	• PD (55) • Lap (62) • PD& LAP (21/55)	Mortality 90 days after intervention		PD: 19/55 (34.5%) Lap: 22/62 (35.5%) p-value =0.92	21/55 patients treated with primary PD required a salvage LAP. No S.S difference in mortality between groups (p=0.92) Type of surgery doesn't influence survival outcome in preterm infants with NEC. No advantage between either technique
Rees et al. [2] 2008; (NET trial) Multicentre Study UK, Europe, Australia, New Zealand & Asia	RCT	69	26 weeks	<1000 gm	• PD (35) • Lap (34) • PD+ Lap (26/35)	Survival at 1 and 6 months after intervention	PD:18/35 (51.4%) Lap: 21/33(63.6%) PD alone: 4/35 P>0.05	PD: 14/35 Lap: 11/33 p-value >0.05	26/35 (74%) of neonates treated with PD required delayed lap. 4//35 (11%) survived PD alone. No difference in outcomes between the groups (p>0.05) If a drain is inserted, lap should be considered.
Blakely et al. [3] 2005; Multicentre cohort, USA (NICHD Neonatal Research Network)	Prospective Cohort	156	23-31 weeks	<1000 gm	• PD (80) • Lap (76) • PD + Lap (18)	Mortality		PD: 24/38 (63%) Lap: 29/58 (50%)	Treatment was not a significant variable in predicting mortality. Need for more RCTs
Zenciroglu et al. [4] 2005; Turkey	Retrospective Review	25			• PD (15) • Lap (10)	Survival	PD: 8/15 PD+ Lap: 3/4	Lap: 8/10	PD more effective than Lap. Lap should be used in cases infants unresponsive to PD
Nobel et al. [5] 2001; USA	Retrospective Review	40	23-32 weeks	<1500 gm	• PD (8) • Lap (32)		PD:4/8 Lap:26/32	PD: 4/8 Lap: 6/32	PD useful adjunct but not definitive therapy. May be useful in stabilizing patients before LAP.
Sharma et al. [6] 2004; USA	Prospective Review	78	26 weeks	<1200 gm	• PD (32) • Lap (46)	Mortality		PD: 15/32 Lap: 20/46 p-value >0.05	Lap better choice and should be chosen when PD fails. No SS significance differences in mortality outcome observed between groups (p>0.05)

Dimmitt et al. [7] 2000; USA	Retrospective Review	26	23.74-27.8 weeks	524-920 gm	• PD (17) • Lap (9)	Survival	PD only: 7/17 (41%) Lap: 5/9 (56%) p-value =0.68	PD:10/17 (PD alone: 6 Salvage Lap: 4) Lap: 4/9	Four patients in PD group underwent salvage Lap. All died. Patient did not benefit from salvage Lap No SS differences in survival outcome seen between groups (p=0.68)
Hull et al. [8] 2014; USA	Prospective Cohort	188,703	26.9-29 weeks	401-1500 gm	• Surgery (8,935) • Lap (6,131) • PD (1521) • PD & Lap (1283)	Mortality		Lap: 31% PD: 50% PD & Lap: 34%	NEC mortality was inversely related to birth weight. As birth weight increased mortality decreased. Lap alone (31%) and Lap with PD (34%) had similar mortalities, whereas PD alone was associated with higher mortality 50% than LAP group (31%) (p<0.0001). Preference among surgeons for Lap as compared to PD.
Wahid et al. [9] 2011; Saudi Arabia	Retrospective Reviews	32	25 weeks	<1000 gm	• PD (17) • Lap (15)		Lap: 11/15 (73.4%) PD: 8/17 (47.1%)	LAP: 4/15 (26.6%) PD: 9/17 (52.9%) p-value =0.14	Increased survival (73.4%) in the laparotomy group when compared with (47.1%) in the PD group even though not SS difference between groups (p=0.14)
Ahmed et al. [10] 1998; Canada	Retrospective Reviews	45	24.2-39 weeks	846-2271 gm	• PD (4) • PD & Lap (19) • Lap (22)	Mortality		PD drainage only: 3/4 (75%) PD& Lap: 10/19 (53%) Lap: 3/22 (14%)	For peritoneal drain neonates did not show a statistically significant benefit in terms of morbidity or mortality over those who had a primary laparotomy. Majority of critically ill infants with NEC will require laparotomy.

effect indicating a small favor to laparotomy in terms of survival. However, this difference between the PD and LAP treatment is not statistically significant (RR:1.20 [0.99,1.46]. at 5% significant level (Figure 3).

In this funnel plot comparing PD with Laparotomy, 95% of the studies are distributed within the funnel indicating no publication bias [20,22].

Discussion

The purpose of this study was to examine the efficacy of PD and

Table 2: A) Quality assessment results according to JBI critical appraisal list for RCTs.

Author	Reviewer	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Max Score	Overall Score
Rees, 2008	A	✓	✓	✓	N/A	N/A	N/A	✓	✓	✓	✓	✓	✓	N/A	9	9/9
Rees, 2008	B	✓	✓	✓	N/A	N/A	N/A	✓	✓	✓	✓	✓	✓	N/A	9	9/9
Moss, 2006	A	✓	✓	✓	N/A	N/A	N/A	✓	✓	✓	✓	✓	✓	✓	10	10/10
Moss, 2006	B	✓	✓	✓	N/A	N/A	N/A	✓	✓	✓	✓	✓	✓	✓	10	10/10

Table 2: B) Quality assessment results according to JBI critical appraisal list for Cohort studies.

Author	Reviewer	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Max Score	Overall Score
Blakely, 2005	A	✓	✓	✓	☒	✓	N/A	✓	✓	✓	☒	✓	10	8/10
Blakely, 2005	B	✓	✓	✓	☒	✓	N/A	✓	✓	✓	☒	✓	10	8/10
Hull, 2014	A	✓	✓	✓	✓	✓	N/A	✓	☒	☒	☒	✓	10	7/10
Hull, 2014	B	✓	✓	✓	✓	✓	N/A	✓	☒	☒	☒	✓	10	7/10

Table 2: C) Quality assessment results according to JBI critical appraisal list for Retrospective chart reviews.

Author	Reviewer	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Max Score	Overall Score
Ahmed,1998	A	✓	✓	✓	✓	✓	✓	☒	0	✓	✓	10	8/10
Ahmed,1998	B	✓	✓	✓	✓	✓	✓	☒	0	✓	✓	10	8/10
Dimmitt, 2000	A	✓	✓	0	✓	✓	✓	✓	✓	✓	✓	10	9/10
Dimmitt, 2000	B	✓	✓	0	✓	✓	✓	✓	✓	✓	✓	10	9/10
Noble, 2001	A	☒	☒	☒	✓	✓	✓	0	0	0	0	10	3/10
Noble, 2001	B	☒	☒	☒	✓	✓	✓	0	0	0	0	10	3/10
Sharma, 2004	A	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10	10/10
Sharma, 2004	B	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10	10/10
Zeniciroglu,2005	A	✓	✓	✓	✓	✓	✓	☒	0	✓	✓	10	8/10
Zeniciroglu,2005	B	✓	✓	✓	✓	✓	✓	☒	0	✓	✓	10	8/10
Wahid, 2011	A	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10	10/10
Wahid, 2011	B	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10	10/10

Key: ✓ -Yes; ☒- No; 0- Unclear; N/A- Not Applicable
Score: Yes-1; No- 0; Unclear-0; N/A-0.

laparotomy in LBW neonates suffering from NEC. According to findings of ten publications identified, nine studies (9/10) reported that Laparotomy resulted in higher survival in patients as compared to PD [5,6,11-17] and only one study (1/10), a chart review documented that PD was more effective, although four patients required salvage laparotomy at a later date with three survivors [18]. This is consistent with a recent meta-analysis of 5 studies (3 cohorts and 2 RCTs) undertaken by Sola et al. which demonstrated that PD is associated with a 55% increase in mortality as compared to Laparotomy (OR: 1.55; 95% CI: 1.08-2.22; I^2:32%) [23]. More evidence was provided by a meta-analysis performed by Moss et al. comparing the effectiveness of PD and LAP in neonates with NEC in 10 retrospective studies. According to the authors, the findings were inconclusive due to heterogeneity between sample size, gestational age and birth weight between the intervention groups [4]. No significant benefit or harm of PD over LAP was also documented in a Cochrane systematic review undertaken by Rao et al.

Contrarily, Zenciroglu et al. [18] observed an increase in survival for neonates >1500 g with NEC undergoing primary PD. Factors such as the patient's gestational age, weight, clinical status as well as the extent of the disease influence the choice and outcome of the surgical intervention [3]. It was documented that NEC mortality is inversely related to birth weight and gestational age [14,24]. More specifically, for every 100 g increase in birth weight, overall mortality from surgical intervention (PD or Laparotomy) declined by 36% [14]. Therefore, in neonates with gestational age >30 weeks and body weight >1500 g, PD alone may be effective. Previous studies undertaken in premature neonates (<1000 g) with NEC, utilizing PD as the primary option reported higher mortality rate as compared to initial LAP. And in cases where patients deteriorated after PD or due to the formation of intestinal strictures, surgeons resorted to salvage LAP as the next step [25-29]. In contrast, other studies documented that in extremely low birth weight babies (<1000 g), general anesthesia and major abdominal surgery may cause hemodynamic instability. In this case, it was suggested that PD may be used as a 'rescue' option to stabilize patients until laparotomy is feasible [29,30]. On the other hand, it has been proposed that surgical choice should be based on the disease and not on birth weight [16]. Another factor that might explain discrepancies between studies reviewed is that patients with intestinal perforation were more likely to have PD and those with NEC, initial LAP laparotomy [12]. PD may be the most suitable surgical intervention in patients suffering from isolated perforation rather than perforated NEC, hence explaining the higher survival rate documented among studies in this group [31,32].

Recent studies have reported increased survival in neonates undergoing LAP, thus advocating that this surgical method should be the treatment of choice in VLBW neonates with intestinal perforation due to NEC [33-36]. As identified from the literature search, most

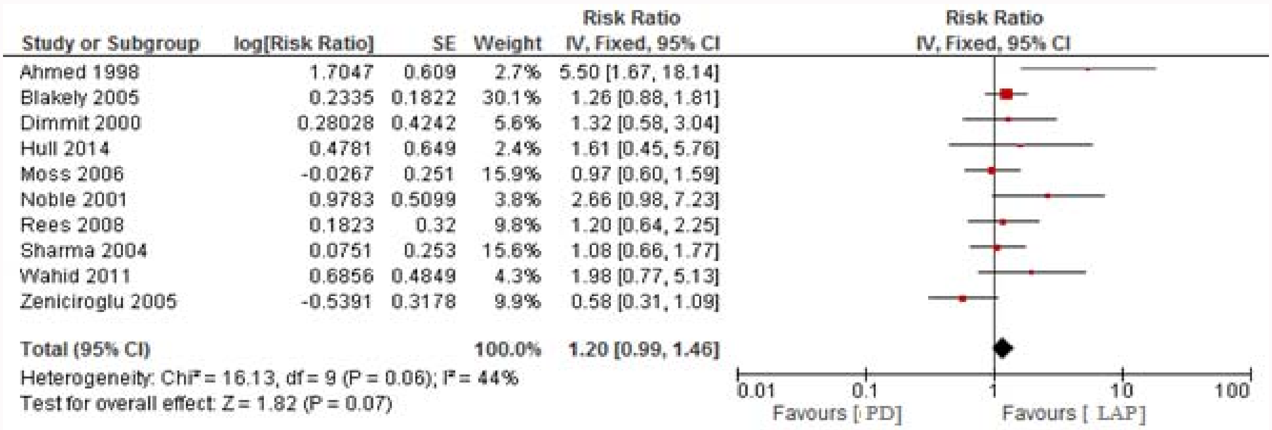

Figure 2: Forest plot comparing PD versus LAP for 'mortality' outcome.

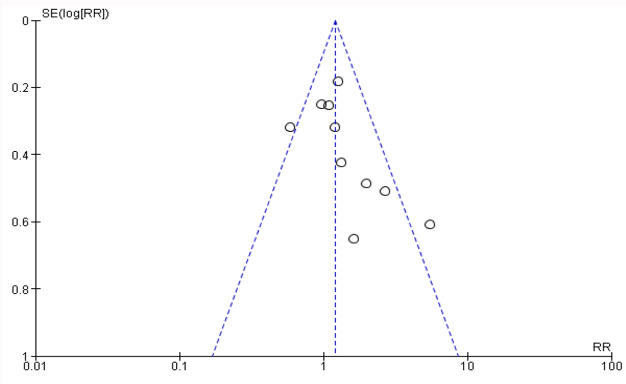

Figure 3: Funnel plot comparing PD versus LAP for 'mortality' outcome.

of this evidence is from retrospective chart reviews which can only propose hypotheses to be tested and validated by the gold standard, randomized clinical trials. Nevertheless, there is light at the end of the tunnel. At present, we are awaiting data from two recent clinical trials, NEST (ClinicalTrials.gov NCT01029353) and STAT (ACTRN12611000317998/ISRCTN01700960) conducted in neonates suffering with NEC. NEST, entitled 'Laparotomy *vs.* Drainage for Infants with Necrotizing Enterocolitis' is an on-going RCT. The purpose of this trial is to compare the effectiveness between LAP and PD in the treatment of NEC or Intestinal Perforation (IP) in VLBW (≤ 1000 g). The primary outcome of interest is neurodevelopment. It is anticipated that 300 infants diagnosed with NEC or IP will be enrolled and randomized into two groups, undergo initial LAP or PD and possibly salvage LAP in the case of deterioration. Survivors will be assessed at 18 to 22 months. This trial is due to end on November 2018. The STAT trial (Stoma or intestinal anastomosis for necrotizing enterocolitis of the neonate) was completed in November, 2013. This international multicenter RCT involved centers in Canada, USA, UK, Latvia, Italy, Netherlands, Sweden and Serbia. The hypothesis tested is whether primary anastomosis after intestinal resection aids recovery of the intestine and reduces time to full enteral feeding in neonates with NEC. The primary outcome measure is duration of parental nutrition and neurodevelopment. Eighty patients were randomized and allocated into two groups. Prior to the interventions, all neonates underwent primary LAP after which a stoma formation was conducted in patients of group one and primary anastomosis in group two. Both clinical trials will provide further evidence for the surgical management of NEC in VLBW neonates.

Limitations/Strengths

Strength of this study is the use of PRISMA guidelines for the systematic approach in reporting and collating of evidence for this review. Another one is the up-to-date extensive database search including international clinical trial registries RCTs and observational studies. Moreover, critical assessment of the evidence reported in the ten publications using JBI quality assessment tool to determine risk of bias is an asset. Finally, the statistical assessment of data using Cochrane's Review Manager Software to conduct the meta-analysis results in an overall quantitative measure of survival assessment.

Meta-analysis of the ten publications revealed moderate heterogeneity between study methodologies which was confirmed statistically using the I^2 statistic. Furthermore, no publication bias was indicated using the funnel plot. A possible explanation for the inconsistency in the findings reported might be due to heterogeneity among study design, sample size, infants' age and number of patients allocated to each intervention including statistical tests applied in evaluating significance of the results. Confounding factors such as birth weight was not taken into account in all studies. Only, one study evaluated the efficacy of PD in neonates (<1000 g) as compared to those ≥ 1500 g [11]. Another limitation may be the length of the necrotic bowel which might contribute to the survival of the patient [34,37]. Blakely et al. [12] noted that the mean length of normal small bowel was greater in survivors than in non-survivors.

Conclusion

The purpose of this meta-analysis was to provide the most recent clinical evidence on the best surgical intervention, namely PD versus LAP in the management of NEC in neonates. Based on the evidence from the extensive bibliographic search of nine databases, data from 10 publications suggest that LAP may be deemed the most appropriate and effective surgical intervention indicating higher survival rate/lower mortality in LBW neonates suffering from NEC as compared to primary PD. PD might be useful as an adjunct therapy to LAP. However, future RCTs are warranted to provide more solid evidence in support of the findings documented in this systematic review before definite guidelines can be disseminated regarding the surgical management of NEC in LBW and premature neonates.

Key Points

- NEC is one of the most devastating diseases in LBW neonates

- Controversy exists concerning the best surgical intervention for this disease
- For neonate <1000 gram and unstable first choice primary PD and when regains stability, salvage LAP.
- Lap best choice when PD fails
- For neonates >1000 grams, best choice LAP

References

1. Lin PW, Stoll BJ. Necrotising enterocolitis. Lancet. 2006;368(9543):1271-83.
2. Zani A, Eaton S, Puri P, Rintala R, Lukac M, Bagolan P, et al. International survey on the management of necrotizing enterocolitis. Eur J Pediatr Surg. 2015;25(1):27-33.
3. Pierro A. The surgical management of necrotising enterocolitis. Early Hum Dev. 2005;81(1):79-85.
4. Moss RL, Dimmitt RA, Henry MC, Geraghty N, Efron B. A meta-analysis of peritoneal drainage versus laparotomy for perforated necrotizing enterocolitis. J Pediatr Surg. 2001;36(8):1210-3.
5. Moss RL, Dimmitt RA, Barnhart DC, Sylvester KG, Brown RL, Powell DM, et al. Laparotomy versus peritoneal drainage for necrotizing enterocolitis and perforation. N Engl J Med. 2006;354(21):2225-34.
6. Rees CM, Eaton S, Kiely EM, Wade AM, McHugh K, Pierro A. Peritoneal drainage or laparotomy for neonatal bowel perforation? A randomized controlled trial. Ann Surg. 2008;248(1):44-51.
7. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;6(7):e1000097.
8. Liberati A, Altman D, Tetzlaff J, Mulrow C, Gøtzsche P, Ioannidis J. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med. 2009;6(7):e1000100.
9. JBI. Joanna Briggs Institute: Critical Appraisal Tools Australia: University of Adelaide; 2017.
10. Holly C, Salmond S, Saimbert M. Comprehensive systematic review for advanced practice nursing: Springer Publishing Company; 2016.
11. Ahmed T, Ein S, Moore A. The role of peritoneal drains in treatment of perforated necrotizing enterocolitis: Recommendations from recent experience. J Pediatr Surg. 1998;33(10):1468-70.
12. Blakely ML, Lally KP, McDonald S, Brown RL, Barnhart DC, Ricketts RR, et al. Postoperative outcomes of extremely low birth-weight infants with necrotizing enterocolitis or isolated intestinal perforation: A prospective cohort study by the NICHD Neonatal Research Network. Ann Surg. 2005;241(6):984-9; discussion 989-94.
13. Dimmitt RA, Meier AH, Skarsgard ED, Halamek LP, Smith BM, Moss RL. Salvage laparotomy for failure of peritoneal drainage in necrotizing enterocolitis in infants with extremely low birth weight. J Pediatr Surg. 2000;35(6):856-9.
14. Hull MA, Fisher JG, Gutierrez IM, Jones BA, Kang KH, Kenny M, et al. Mortality and management of surgical necrotizing enterocolitis in very low birth weight neonates: A prospective cohort study. J Am Coll Surg. 2014;218(6):1148-55.
15. Noble HGS, Driessnack M. Bedside peritoneal drainage in very low birth weight infants. Am J Surg. 2001;181(5):416-9.
16. Sharma R, Tepas JJ, Mollitt DL, Pieper P, Wludyka P. Surgical management of bowel perforations and outcome in very low-birth-weight infants (< or =1,200 g). J Pediatr Surg. 2004;39(2):190-4.
17. Wahid FN, Al-Onazi M, Mohaidly M, Rawaf A, Otaibi A, Hudhaif J, et al. Peritoneal drainage versus laparotomy as an initial treatment in complicated necrotizing enterocolitis: A single institution experience. Ann Ped Surg. 2013;7(3):97-100.
18. Zenciroğlu A, Çakmak Ö, Demirel N, Baş A, Yılmaz D, Karaman I, et al. Outcome of primary peritoneal drainage for perforated necrotizing enterocolitis: Comparison between laparotomy and drainage. Eur J Pediatr Surg. 2005;15(4):243-7.
19. Collaboration TC. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014: Cochrane Collaboration; 2014.
20. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions: John Wiley & Sons; 2011.
21. Egger M, Smith GD, Phillips AN. Meta-analysis: Principles and procedures. BMJ. 1997;315(7121):1533-7.
22. Sterne JA, Harbord RM. Funnel plots in meta-analysis. Stata J. 2004;4(2):127-41.
23. Sola JE, Tepas JJ, Koniaris LG. Peritoneal drainage versus laparotomy for necrotizing enterocolitis and intestinal perforation: A meta-analysis. J Surg Res. 2010;161(1):95-100.
24. Fitzgibbons SC, Ching Y, Yu D, Carpenter J, Kenny M, Weldon C, et al. Mortality of necrotizing enterocolitis expressed by birth weight categories. J Pediatr Surg. 2009;44(6):1072-5; discussion 1075-6.
25. Demestre X, Ginovart G, Figueras-Aloy J, Porta R, Krauel X, Garcia-Alix A, et al. Peritoneal drainage as primary management in necrotizing enterocolitis: A prospective study. J Pediatr Surg. 2002;37(11):1534-9.
26. Eicher C, Seitz G, Bevot A, Moll M, Goelz R, Arand J, et al. Surgical management of extremely low birth weight infants with neonatal bowel perforation: A single-center experience and a review of the literature. Neonatology. 2012;101(4):285-92.
27. Goyal A, Manalang L, Donnell S, Lloyd D. Primary peritoneal drainage in necrotising enterocolitis: An 18-year experience. Pediatr Surg Int. 2006;22(5):449-52.
28. Tan Y-W, Merchant J, Sharma V, Davies B, Singh S, Stewart R, et al. Extensive necrotising enterocolitis: Objective evaluation of the role of second-look laparotomy in bowel salvage and survival. World J Surg. 2015;39(12):3016-22.
29. Zornoza M, Pelaez D, Romero R, Corona C, Tardáguila A, Rojo R, et al. [Role of peritoneal drainage in necrotizing enterocolitis in critical infants with extremely low birth weight]. Cir Pediatr. 2011;24(3):146-50.
30. Ein SH, Marshall DG, Girvan D. Peritoneal drainage under local anesthesia for perforations from necrotizing enterocolitis. J Pediatr Surg. 1977;12(6):963-7.
31. Hu G, Cassano PA. Antioxidant nutrients and pulmonary function: the third National Health and Nutrition Examination Survey (NHANES III). Am J Epidemiol. 2000;151(10):975-81.
32. Mishra P, Foley D, Purdie G, Pringle KC. Intestinal perforation in premature neonates: The need for subsequent laparotomy after placement of peritoneal drains. J Paediatr Child Health. 2016;52(3):272-7.
33. Argumosa SY, Fernández CM, Gonzálvez PJ, Hernández AE, Baquero CM, Medina MC, et al. [Necrotizing entercolitis and intestinal perforation in very low weight premature infants: Which is the best surgical option?] Cir Pediatr. 2011;24(3):142-5.
34. Gfroerer S, Fiegel H, Schloesser RL, Rolle U. Primary laparotomy is effective and safe in the treatment of necrotizing enterocolitis. World J Surg. 2014;38(10):2730-4.
35. Camberos A, Patel K, Applebaum H. Laparotomy in very small premature infants with necrotizing enterocolitis or focal intestinal perforation: Postoperative outcome. J Pediatr Surg. 2002;37(12):1692-5.

36. Sakellaris G, Partalis N, Dede O, Alegakis A, Seremeti C, Korakaki E, et al. Gastrointestinal perforations in neonatal period: Experience over 10 years. Pediatr Emerg Care. 2012;28(9):886-8.

37. Alexander F, Smith A. Mortality in micro-premature infants with necrotizing enterocolitis treated by primary laparotomy is independent of gestational age and birth weight. Pediatr Surg Int. 2008;24(4):415-9.