Journal of Pediatric Surgery 55 (2020) 1270–1275

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Neonatal Conditions

Multicenter retrospective comparison of spontaneous intestinal perforation outcomes between primary peritoneal drain and primary laparotomy

Samantha Ahle [b,*,1], Faidah Badru [a,h,1], Rachelle Damle [a], Hector Osei [a], Armando Salim Munoz-Abraham [a], Adam Bajinting [g], Maria Estefania Barbian [e], Amina M. Bhatia [d], Cindy Gingalewski [f], Jose Greenspon [a], Nicholas Hamilton [e], David Stitelman [b], Marya Strand [a], Brad W. Warner [c], Gustavo A. Villalona [a]

[a] Section of Pediatric Surgery, Saint Louis University/Cardinal Glennon Children's Medical Center, St. Louis, MO
[b] Section of Pediatric Surgery, Yale University School of Medicine/Yale-New haven Hospital, New Haven, CT
[c] Division of Pediatric Surgery, Washington University School of Medicine/Saint Louis Children's Hospital, St. Louis, MO
[d] Section of Pediatric Surgery, Children's Healthcare of Atlanta, Atlanta, GA
[e] Department of Pediatrics, Emory University School of Medicine, Atlanta, GA
[f] Section of Pediatric Surgery, Oregon Health and Science University, Portland, OR
[g] Section of Pediatric Surgery, Randall Children's Hospital at Legacy Emanuel, Portland, OR
[h] Saint Louis University School of Medicine, Saint Louis, MO

ARTICLE INFO

Article history:
Received 12 March 2019
Received in revised form 5 July 2019
Accepted 10 July 2019

Key words:
Spontaneous intestinal perforation
Peritoneal drain
Necrotizing enterocolitis

ABSTRACT

Purpose: The purpose of our study was to compare outcomes of infants with spontaneous intestinal perforation (SIP) treated with primary peritoneal drain versus primary laparotomy.
Methods: We performed a multi-institution retrospective review of infants with diagnosis of SIP from 2012 to 2016. Clinical characteristics and outcomes were compared between infants treated with primary peritoneal drain vs infants treated with laparotomy.
Results: We identified 171 patients treated for SIP (drain $n = 110$ vs. laparotomy $n = 61$). There were no differences in maternal or prenatal characteristics. There were no clinically significant differences in vital signs, white blood cell or platelet measures, up to 48 h after intervention. Patients who were treated primarily with a drain were more premature (24.9 vs. 27.2 weeks, $p < 0.001$) and had lower median birth weight (710 g vs. 896 g, $p < 0.001$). No significant differences were found in complications, time to full feeds, length of stay (LOS) or mortality between the groups. Primary laparotomy group had more procedures (median number 1 vs. 2, $p = 0.002$). There were 32 (29%) primary drain failures whereby a laparotomy was ultimately needed.
Conclusions: SIP treated with primary drain is successful in the majority of patients with no significant differences in outcomes when compared to laparotomy with stoma.
The level of evidence: III.

Intestinal perforation in the newborn is a neonatal emergency that continues to have associated morbidity and mortality despite advances in critical care [1–4]. It can be associated with prolonged neonatal intensive care unit stays, as well as delayed initiation of enteral feeds. The two most common causes of newborn intestinal perforation are necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP) [5]. The incidence of NEC has been reported to be 6–8% of very low weight (VLBW, <1500 g) infants and extremely low birth weight (ELBW, <1000 g) infants [6]. The incidence of SIP is 2% of VLBW infants and up to 8% of ELBW infants [1,7–9]. Although frequently studied together, they are different disease entities with different pathologies [10,11]. On histologic examination, NEC shows coagulative necrosis and SIP shows isolated hemorrhagic necrosis [12,13]. This has prompted further investigation into determining if the two diseases present differently or affect different groups of infants. Newborns with SIP tend to have younger gestational age and lower birth weight [1,3,12,14]. Additionally, it has been questioned whether factors such as infection, medications (steroid or nonsteroidal anti-inflammatory (NSAID) medications), timing of enteral feeds, or CPAP use contribute to the development of SIP [12].

* Correspond author at: Department of Surgery, Yale University School of Medicine, 330 Cedar Street, FMB 107, New Haven, CT 06519. Tel: +1 203 785 7890; fax: +1 203 737 5209.
E-mail address: samantha.ahle@yale.edu (S. Ahle).
[1] These authors have contributed equally to the manuscript.

https://doi.org/10.1016/j.jpedsurg.2019.07.007
0022-3468/

When considered as one disease entity, spontaneous intestinal perforation has been reported to have a mortality as high as 47% [1–4,15,16]. Prompt diagnosis and intervention for free intraperitoneal air are of the utmost importance. Treatment was initially, and still frequently remains, laparotomy and resection of the affected bowel with stoma formation. However, in the context of NEC, peritoneal drainage was reported as a possible way to intervene, specifically for neonates who were considered too sick to tolerate laparotomy [17]. Since that time many studies have been done to study outcomes of primary laparotomy (PL) versus primary drainage (PD) in neonatal intestinal perforation. Some of these studies have examined drainage as definitive management instead of a temporizing management; no clear conclusion has been made with some studies suggesting primary laparotomy is required and others suggesting drainage is sufficient [2,3,15,16,18,19].

However, studies to date fail to differentiate between infants with SIP and NEC, and with a better understanding that these are different disease processes, it is important to understand if the treatments should be different. The studies that have been done to investigate this are small but show that drainage is a safe option in SIP and is more likely to lead to definitive management than in NEC [11,20–23]. The most recent study from Jakaitis et al. evaluated predictors and hospital outcomes for patients with SIP and demonstrated that PD is a definitive therapy in 75% of the patients. Furthermore, they identified birth weight < 750 g, presentation after 7 days of life and use of NSAID therapy prior to diagnosis as predictors of successful treatment with PD alone [24].

Given the rarity of SIP and the small sizes of previous studies, we performed a multicenter retrospective investigation to compare hospital outcomes between SIP infants undergoing PD versus PL with ostomy creation. We hypothesized that PD placement is a safe and effective technique that is associated with fewer interventions and anesthetic exposures. Finally, we aim to identify pre-, intra- and postoperative predictors for PD failure.

1. Methods

1.1. Study design

After Institutional Review Board approval was obtained a multicenter retrospective review of infants diagnosed with SIP between January 1, 2012 and December 31, 2016 was performed. Using administrative hospital databases and practice databases, 171 patients across the 6 participating institutions were identified. We included infants with pneumoperitoneum, and/or perinatal/spontaneous intestinal perforation who underwent peritoneal drain placement or primary laparotomy. The final diagnosis was determined by the operating surgeon, based on the operative note, which was read in detail for accuracy of diagnosis. We excluded patients diagnosed with NEC prior to intervention, at laparotomy or soon after intervention.

We collected maternal and infant demographics, prenatal and postnatal factors, preoperative, intraoperative and postoperative characteristics, survival, need for further surgical interventions and other clinical outcomes between groups. Subgroup analysis was performed to identify predictors of primary peritoneal drain failure.

1.2. Definitions/data collection

The final diagnosis of spontaneous intestinal perforation was determined by the operating surgeon, based on the operative note. We excluded any patient diagnosed with NEC prior to intervention, at laparotomy or soon after of either intervention. Patients with no pneumoperitoneum were initially diagnosed by abdominal ultrasound. These patients were found to free fluid with debris, consistent with intestinal perforation as per radiologist. We defined complications as enterocutaneous fistula (ECF), sepsis within 14 days from SIP diagnosis, recurrent pneumoperitoneum, stoma prolapse, wound complications (superficial infection, evisceration), incisional hernia, bowel dehiscence (anastomotic breakdown or leak), intraabdominal abscess, stricture, and bowel obstruction. Peritoneal drain was defined as patients treated with drain without laparotomy or stoma creation. Failure of peritoneal drain was defined as development of complications leading to subsequent salvage laparotomy with or without stoma creation.

Study data were collected and managed using REDCap (Research Electronic Data Capture) software hosted by Saint Louis University [27]. All study data were validated both centrally and at each individual institution for completeness of data entry and accuracy. Missing data were obtained to the degree possible, and outliers were confirmed to be accurate.

1.3. Surgical technique

The surgical techniques for PD vary widely from institution to institution and even between surgeons within an institution. Some surgeons report using a single right lower quadrant (RLQ) incision to decompress the abdominal cavity and others use a second counterincision on the patient's abdomen so the drain can be passed through both incisions (Fig. 1). Primary laparotomies may be done at the bedside or in the operating room, always utilizing general anesthesia. Most commonly, an RLQ laparotomy is performed. This allows bowel inspection and creation of a stoma via the same incision.

1.4. Statistics

Statistical analysis was performed using STATA (StataCorp. 2011, Stata Statistical Software: Release 12. College Station, TX). Continuous data were expressed as means or medians with interquartile ranges, and categorical variables were expressed as percentages. For categorical variable comparisons, Pearson's Chi-square test was used. One-way analysis of variance was used to compare continuous data, as appropriate. Multivariable logistic regression was performed for outcomes of interest. Variables were chosen for inclusion in the multivariable model by consensus based on a priori knowledge, or a p-value <0.2 on univariate analysis. A p-value less than 0.05 was considered statistically significant.

2. Results

2.1. Epidemiology

Our final study cohort included 171 patients that met our inclusion criteria, of which 110 patients were treated with PD and 61 patients were treated with PL. At delivery the mean maternal age for was 27.5 years (SD 6.8), 35% were multiple gestations, 57% received prenatal steroids, and 34% of patients were delivered vaginally. About 46% of mothers had histologic chorioamnionitis and 82% had clinical chorioamnionitis reported. Males composed 62% of patients (n = 106). The mean gestational age (GA) was 25.7 weeks (SD 2.4 weeks), and the birth weight median was 760 g (IQR 251) with a range of 380 to 3660 g. Of these, 19 infants (11%) were 1001–2000 g, 5 infants (3%) were 2001–3000 g and 3 infants (2%) were >3000 g. The majority of patients were preterm infants, though 2 were early term gestation at 37 weeks at birth.

Physical exam at diagnosis revealed 89% of patients had a soft, distended, and tender abdomen. Abdominal discoloration (bluish or greenish) was not collected for this study; however, there were 6 patients (3%) with abdominal wall erythema. Diagnosis was made by plain film (X-ray) in 97% of patients and by abdominal ultrasound in 4% of the patients. Furthermore, 6 patients (3%) with final diagnosis of SIP at operation had preoperative radiographic concern for NEC (pneumatosis intestinalis or portal venous gas).

The median day at diagnosis after birth was 6 days (range 0–52 days). Sixty-six percent occurred <7 days after delivery, 32%

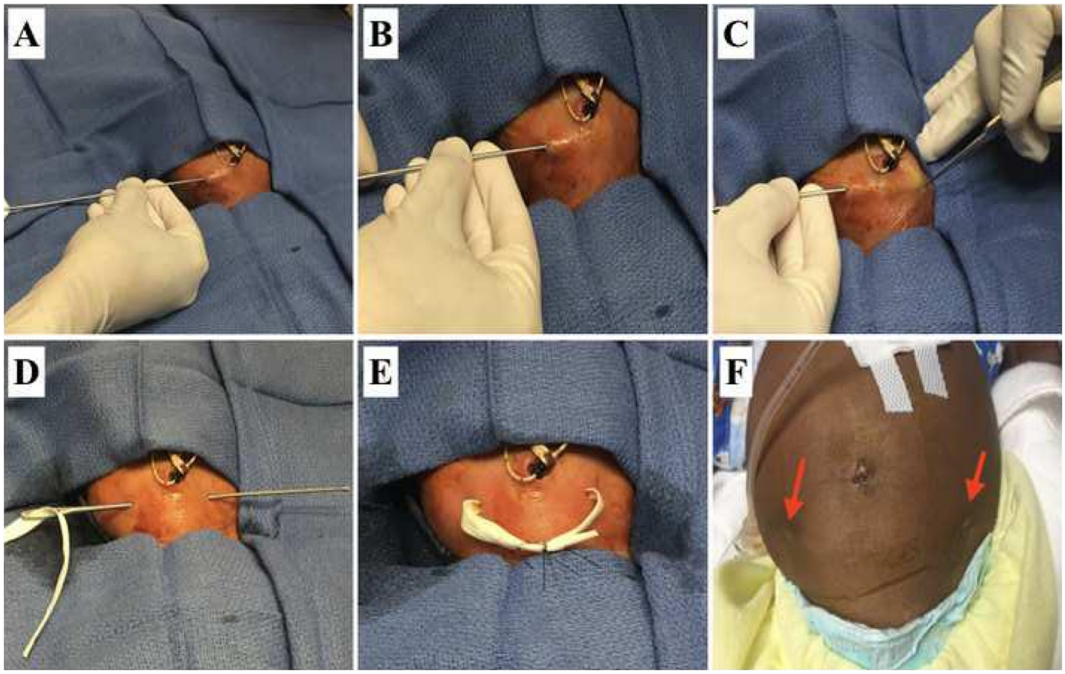

Fig. 1. Primary drain placement. Legend: Drain is passed from RLQ to LLQ using a probe (A, B, C). The probe is pulled out via the LLQ incision (D) and the drain is tied to itself to prevent accidental removal (E). Incisions healed several months later (F). Arrows mark surgical scars.

occurred between 8 and 21 days after delivery and 2% occurred beyond 21 days after delivery. The mean day feeds were introduced after delivery was 8 days. Thirty-eight percent of patients received NSAIDs prior to the perforation and 26% received postnatal steroids. Thirty-four patients (20%) had severe IVH. However, 29 of these (85%) were diagnosed prior to the SIP diagnosis. The primary surgical procedure was carried out at the bedside in 57% of all patients and the most common peritoneal fluid characteristic was "meconium stained/fecal." At the time of diagnosis 18% of patients were not intubated and 51% of patients were on vasopressor medication. Of these, 39 were on dopamine, 3 were on epinephrine and 46 were on hydrocortisone. Overall, there were 76 surgical complications (44%) reported for all patients. The median length of stay (LOS) was 101 days (IQR 60); the median time to full feeds following the surgical intervention was 47 days (IQR 45). The inpatient mortality was 20% ($n = 35$).

2.2. Group comparisons

2.2.1. Prenatal characteristics

The groups were equivalent with regards to pregnancy characteristics, including maternal age, multiple gestations, duration of rupture of membranes, abnormal placental blood flow, mode of delivery and antenatal steroid exposure (Table 1).

2.2.2. Postnatal characteristics

Comparison of preoperative characteristics showed that patients with drain placement had lower APGARs at 1 and 5 min, were more premature at delivery (PD 24.9 vs PL 27.2 weeks completed gestation, $p < 0.0001$), had lower birth weights (median PD 710 g vs PL 896 g, $p < 0.0001$) and had higher rate of severe intraventricular hemorrhage (PD 26% vs PL 8%, $p = 0.004$). We also noted that only half of the patients with drain versus the majority of patients with laparotomy perforated <7 days from birth (PD 57% vs PL 80%, $p = 0.002$). We found that PD patients received more steroids (dexamethasone or hydrocortisone) after birth compared to PL patients (PD 35% vs PL 11%, $p = 0.005$). There were no clinically significant differences between group vital signs, physical exam, image findings, white blood cell and platelet counts, blood gas measurements, vasopressor use, and mechanical ventilation.

2.2.3. Intraoperative group comparison

Most patients with PD underwent intervention at the bedside compared to the PL group (PD 99% vs PL 37%, $p < 0.001$). No differences in fluid characteristics upon intervention were identified between groups. "Meconium-stained/fecal" was the most commonly reported (56%). In

Table 1
Demographics by primary procedure type.

Infant Characteristics	Drain ($n = 110$)	Laparotomy ($n = 61$)	*P* Value
Apgar 1 min, mean (SD)	3.1 (2.19)	4.2 (2.6)	0.005
Apgar 5 min, mean (SD)	5.6 (2.2)	6.6 (2.1)	0.006
Histologic Chorioamnionitis (%)	47 (42)	32 (52)	0.055
Clinical Chorioamnionitis (%)	90 (82)	51 (84)	0.57
Race (%)			0.5
White	50 (45)	27 (44)	
African-American	45 (41)	20 (33)	
Other	10	10	
Ethnicity (Hispanic)	4	5	
Male (%)	67 (61)	41 (67)	0.41
Gestational age (weeks), mean (SD)	24.9 (1.3)	27.2 (3.3)	0.0001
Birth Weight (g) median, (IQR)	705 (275)	895 (278)	0.0001
Weight at diagnosis, *n* (%)			0.001
<750 g	77 (71)	22 (42)	
751–1000 g	30 (28)	12 (20)	
1001–1500 g	2 (1.83)	16 (26)	
>1501 g	1 (0.9)	11 (18)	
Comorbid condition, *n* (%)	48 (44)	34 (56)	0.129
Cardiac	8 (7.27)	7 (11)	
Genetic	2 (1.82)	2 (3.28)	
CNS	19 (17)	9 (15)	
Renal	2 (1.82)	2 (3.28)	
Severe IVH during hospitalization, *n* (%)	29 (26)	5 (8.2)	0.004
Before diagnosis	21 (72)	4 (80)	
After diagnosis	8 (28)	1 (20)	
Received NSAIDs, *n* (%)	48 (45)	17 (28)	0.09
Received postnatal steroids, *n* (%)	38 (35)	7 (11)	0.005

Abbreviations: *n*, number; SD, standard deviation; g, grams; IQR, interquartile range; CNS, central nervous system; IVH, intraventricular hemorrhage; NSAIDs, nonsteroidal anti-inflammatory drugs.

the PD group, there were 6 patients (5%) that were never intubated before, during or up to 48 h after intervention. During laparotomy, intestinal perforation was identified in the terminal ileum in 55 patients (90%), in the cecum in 4 patients (7%) and in the jejunum in 2 patients (3%).

2.3. Postoperative outcomes

Postoperative clinical outcomes between the two groups were similar. Thirty-two patients (29%) in the PD group required a salvage laparotomy owing to drain failure. Median time to salvage laparotomy was 19 days (IQR 61). There were no differences in reasons for salvage laparotomy when compared to timing of event. Early salvage laparotomy (<14 days) was because of abscess formation, recurrent pneumoperitoneum, sepsis and bowel obstruction. Late salvage laparotomy >14 days, was because of abscess formation, bowel obstruction, ECF and recurrent pneumoperitoneum. Six patients (10%) of the PL group required reexploration after initial laparotomy. The reasons for reexploration in this group were stricture formation at the stoma site with secondary bowel obstruction in 4 patients (mean time 45 days) and evisceration in the other 2 patients (mean time 7 days). The median additional procedures after initial intervention for PL patients was significantly higher (PD 1 vs PL 2, $p = 0.002$), most often because of standard ostomy takedown. Complications by group are reported in Table 2. Recurrent pneumoperitoneum was significantly higher for patients undergoing drain placement (PD 18% vs PL 2%, $p = 0.002$), of which 3 were managed successfully with repeat drain placement. There were no significant differences in time to full feeds, length of stay or mortality between the groups (Table 3).

2.4. Necrotizing enterocolitis

Six patients developed NEC after initial management of SIP following a period of full feeds and normal recovery. In the PL group, 2 patients had *NEC totalis* 20 days and 5 weeks later, respectively. One patient had surgical NEC 3 months after SIP, and another patient had medical NEC 2 months after SIP. In the PD group, there were 2 patients that had recovered from initial SIP and were diagnosed with medical NEC 6 weeks and 5 months later, respectively.

2.5. Subgroup analysis: predictors of drain failure

Thirty-two patients (29%) required salvage laparotomy for primary drain failures. There were no significant differences in demographics, prenatal or postnatal characteristics as predictors of failure identified in univariate or multivariate analysis. Drain failure patients had longer time to full feeds and longer LOS.

Table 2
Spontaneous intestinal perforation complications.

	Drain ($n = 110$)	Laparotomy ($n = 61$)	*P* Value
ECF, *n* (%)	4 (3.6)	0	0.1
Sepsis within 14 days, *n* (%)	13 (12)	3 (4.9)	0.1
Recurrent pneumoperitoneum, *n* (%)	20 (18)	1 (1.6)	0.002
Stoma prolapse, *n* (%)	2 (1.8)	6 (9.8)	-
Wound complication, *n* (%)	1 (0.9)	1 (1.6)	0.6
Evisceration, *n* (%)	3 (2.7)	1 (1.6)	0.6
Incisional hernia, *n* (%)	1 (0.9)	0	0.4
Bowel dehiscence,[a] *n* (%)	0	1 (1.6)	-
Intraabdominal abscess, *n* (%)	2 (1.8)	1 (1.6)	0.9
Stricture, *n* (%)	0	2 (3.2)	0.056
Bowel obstruction, *n* (%)	6 (5.4)	4 (6.5)	0.7
Total	52 (47)	24 (39)	0.3

Abbreviations: *n*, number; SD, standard deviation; ECF, enterocutaneous fistula.
[a] Bowel dehiscence: anastomotic breakdown or leak.

3. Discussion

Distinction between SIP and NEC remains a controversial topic, despite significant epidemiological differences between these conditions. The traditional or standard definition of SIP is reported as spontaneous intestinal perforation that affects preterm infants (VLBW and ELBW) and is typically located at the terminal ileum, although it can occur in the cecum or jejunum [7,12,25,26]. Interestingly, we found several patients weighing >1500 g at diagnosis and 2 patients born at term. Upon presentation, the diagnosis is considered in patients with sudden abdominal distention, bluish abdominal wall discoloration and radiographic findings of pneumoperitoneum in the absence of pneumatosis or portal venous gas [3,12,28]. However, up to 40% of patients with perforated NEC have no pneumatosis on imaging, but these patients usually have a different clinical presentation. Multiple studies have shown that SIP patients are significantly more premature, have smaller birth weight, and are younger age at presentation [3,5,11,14,16]. Also, Blakely et al. demonstrated that they could correctly classify SIP versus NEC in 95% of the cases based on abdominal radiographic findings and the patient's age at presentation [3]. However, our study was not set out to evaluate accuracy of diagnosis by surgeons. We already knew these patients had an SIP diagnosis as determined by the operative surgeon.

This cohort represents the largest review of infants with the diagnosis of SIP in the literature, using patient records and clinical variables. Multiple studies have found an association with NSAID use and SIP [29,30]; only 38% of our patients had received it prior to the perforation. The main reasons to differentiate these two conditions are their differing outcomes and mortality. Reported successful primary drain rates for NEC vary from 20% to 50%, whereas SIP patients are treated successfully in up to 75% of the cases [3,24]. In the current cohort of infants with SIP, 70% of patients were successfully treated with a primary peritoneal drain. Fisher et al., using the Vermont Oxford Network (VON) database, demonstrated that the mortality in neonates with laparotomy-confirmed SIP is significantly lower when compared to NEC patients (SIP 19% vs. NEC 38%, $p < 0.0001$) [31]. This is similar to the mortality found in the current cohort (20%) and previous important prospective and retrospective studies. [3,24,32].

It is difficult to preoperatively choose the best surgical therapy owing to the difficulty in clear diagnosis. The main purpose of this study was to compare hospital outcomes between SIP infants undergoing primary PD versus primary PL. Primary laparotomy has been the most traditional approach, with more than 60% of VLBW neonates suffering complications associated with stoma creation [33]. The benefits of PD include bedside exploration, avoidance of stoma complications, and potential avoidance of general anesthesia and elimination of a second operation for stoma takedown. These data support PD as a definitive therapy in infants with SIP, as most of these patients recovered without any further surgical intervention. However, there are data to support the use of primary anastomosis as the definitive treatment for SIP; this would minimize the issues related to further surgical interventions [12,34].

Even though prenatal characteristics were similar between PD and PL groups, these data revealed that patients with primary drain placement were more premature at delivery, had lower birth weights and were less than 750 g at diagnosis. These differences were likely related to surgeons' bias across all institutions to perform drain placement for smaller, more premature infants, irrespective of clinical instability. Most PD placements were performed at the bedside, and six patients were never intubated for this intervention. We believe the main reasons for performing PD or PL at the bedside are usually related to patient size and/or clinical status. Also, most PD patients do not require general anesthesia or operating room staff. In our series, most PD placements were performed at the bedside owing the small patient size, regardless of patient stability, while PL cases performed at the bedside were likely deemed too small or unstable to go to the operating room. Interestingly, there are data to support this practice. Several studies have documented

Table 3
Outcomes by group.

	Drain ($n = 110$)	Laparotomy ($n = 61$)	P Value
Time to first complication (days), median (IQR)	8.5 (8.5)	13 (79)	0.044
Time to first additional procedure (days), median (IQR)	19 (61)	63 (48)	0.001
Days until full feeds (from procedure), median (IQR)	51 (32)	43 (58)	0.3
Length of stay (days), median (IQR)	112 (56)	90 (65)	0.1
Inpatient mortality, *n* (%)	26 (23)	9 (15)	0.1

Abbreviations: *n*, number; SD, standard deviation; IQR, interquartile range.

significant transport-related complications for VLBW and ELBW infants. These patients are at increased risk of hypothermia, deterioration in oxygenation parameters, ventilation parameters and platelet counts. When possible, bedside procedures may help ameliorate some of these complications for these critically ill patients [35–37]. Despite the statistical differences between groups regarding vital signs, laboratory characteristics, and vasopressor use before the procedure, these differences were not clinically significant. Postoperative clinical outcomes were also similar. Thirty-two patients (29%) in the PD group required a salvage laparotomy owing to drain failure. Only 6 patients (10%) of the PL group required reexploration after initial laparotomy owing to complications. As expected, the median number of additional procedures following PL was significantly higher owing to standard ostomy takedown. The PD group had a significantly higher recurrent pneumoperitoneum. There was no significant difference in time to full feeds, length of stay or mortality between the groups. The data revealed that 6 patients in the PL group and 2 patients in the PD group developed NEC after they had recovered from management of SIP and had been on full feeds.

A subgroup analysis was performed in order to better understand patients that would benefit from a primary peritoneal drain. No predictors were significantly associated with failure or success despite the cohort size. There were no significant differences in demographics, prenatal or postnatal characteristics using univariate or multivariate analysis to predict primary drain success. However, drain failure patients had longer time to full feeds and longer LOS.

There are many limitations to our study. This is a retrospective review across multiple centers, where uncontrolled variables can be systematically different owing to institutional practices (feeding, NSAID use, etc.) or surgical trends. This study was intended as a comparison between SIP treatment groups and not to differentiate SIP from NEC. Patients with a final diagnosis other than SIP were excluded. The diagnosis of SIP in the PD group was assumed but not surgically established. Without direct visualization of the affected bowel, this will remain a substantial limitation of any study involving SIP and PD. This an important consideration, since potentially missing NEC could lead to worse outcomes owing to necrotic bowel, sepsis and death [3,5,11,13,14,16]. However, all cases of NEC in our study cohort were diagnosed after they had recovered from their initial management of SIP. Though previous studies have demonstrated preoperative diagnostic accuracy (13), this will always remain unknown. Finally, the main limitation of our study was the likely surgeons' bias across all institutions to perform primary drains for smaller and more premature infants. Despite this presumed bias, the PD group did as well as the PL group postoperatively without increased need for vasopressor support and similar time to feeds.

This study brings us a step closer towards understanding SIP as a distinct clinical entity with significant epidemiological, clinical and radiological differences features. SIP also has significantly different outcomes compared to NEC. This study should help shape future prospective trials to determine best treatment for this condition.

In conclusion, SIP treated with primary drain is successful in the majority of patients with no significant differences in outcomes when compared to laparotomy with stoma. Even though LOS in drain failure patients was increased, salvage laparotomy is safe and it does not mean a death sentence.

No conflict of interest.
No acknowledgments.

References

[1] Blakely ML, Tyson JE, Lally KP, et al. NICHD Neonatal Research Network. Laparotomy versus peritoneal drainage for necrotizing enterocolitis or isolated intestinal perforation in extremely low birth weight infants: outcomes through 18 months adjusted age. Pediatrics 2006;117:e680–7.
[2] Stokes SM, Iocono JA, Draus Jr JM. Peritoneal drainage as the initial management of intestinal perforation in premature infants. Am Surg 2014;80:851–4.
[3] Blakely ML, Lally KP, McDonald S, et al. NEC Subcommittee of the NICHD Neonatal Research Network. 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;241:984–9 [discussion 989–94].
[4] Uceda JE, Laos CA, Kolni HW, et al. Intestinal perforations in infants with a very low birth weight: a disease of increasing survival? J Pediatr Surg 1995;30:1314–6.
[5] Broekaert I, Keller T, Schulten D, et al. Peritoneal drainage in pneumoperitoneum in extremely low birth weight infants. Eur J Pediatr 2018;177:853–8.
[6] Stoll BJ, Hansen NI, Bell EF, et al. Practices, morbidity, and mortality of extremely preterm neonates, 1993–2012. Obstet Gynecol Surv 2016;71:7–9.
[7] Meyer CL, Payne NR, Roback SA. Spontaneous, isolated intestinal perforations in neonates with birth weight less than 1,000 g not associated with necrotizing enterocolitis. J Pediatr Surg 1991;26:714–7.
[8] Alpan G, Eyal F, Vinograd I, et al. Localized intestinal perforations after enteral administration of indomethacin in premature infants. J Pediatr 1985;106:277–81.
[9] Kawase Y, Ishii T, Arai H, et al. Gastrointestinal perforation in very low-birthweight infants. Pediatr Int 2006;48:599–603.
[10] Eicher C, Seitz G, Bevot A, 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;101:285–92.
[11] Tiwari C, Sandlas G, Jayaswal S, et al. Spontaneous intestinal perforation in neonates. J Neonatal Surg 2015;4:14.
[12] Pumberger W, Mayr M, Kohlhauser C, et al. Spontaneous localized intestinal perforation in very-low-birth-weight infants: a distinct clinical entity different from necrotizing enterocolitis. J Am Coll Surg 2002;195:796–803.
[13] de Haro Jorge I, Prat Ortells J, Albert Cazalla A, et al. Long term outcome of preterm infants with isolated intestinal perforation: a comparison between primary anastomosis and ileostomy. J Pediatr Surg 2016;51:1251–4.
[14] Adderson EE, Pappin A, Pavia AT. Spontaneous intestinal perforation in premature infants: a distinct clinical entity associated with systemic candidiasis. J Pediatr Surg 1998;33:1463–7.
[15] Rees CM, Eaton S, Kiely EM, et al. Peritoneal drainage or laparotomy for neonatal bowel perforation? A randomized controlled trial. Ann Surg 2008;248:44–51.
[16] Rao SC, Basani L, Simmer K, et al. Peritoneal drainage versus laparotomy as initial surgical treatment for perforated necrotizing enterocolitis or spontaneous intestinal perforation in preterm low birth weight infants. Cochrane Database Syst Rev 2011; 6:CD006182.
[17] Ein SH, Marshall DG, Girvan D. Peritoneal drainage under local anesthesia for perforations from necrotizing enterocolitis. J Pediatr Surg 1977;12:963–7.
[18] Noble HGS, Driessnack M. Bedside peritoneal drainage in very low birth weight infants. Am J Surg 2001;181:416–9.
[19] Sharma R, Tepas JJ, Mollitt DL, et al. Surgical management of bowel perforations and outcome in very low-birth-weight infants (≤1,200 g). J Pediatr Surg 2004;39:190–4.
[20] Rovin JD, Rodgers BM, Burns RC, et al. The role of peritoneal drainage for intestinal perforation in infants with and without necrotizing enterocolitis. J Pediatr Surg 1999;34:143–7.
[21] Cass DL, Brandt ML, Patel DL, et al. Peritoneal drainage as definitive treatment for neonates with isolated intestinal perforation. J Pediatr Surg 2000;35:1531–6.
[22] Emil S, Davis K, Ahmad I, et al. Factors associated with definitive peritoneal drainage for spontaneous intestinal perforation in extremely low birth weight neonates. Eur J Pediatr Surg 2008;18:80–5.
[23] Buchheit JQ, Stewart DL. Clinical comparison of localized intestinal perforation and necrotizing enterocolitis in neonates. Pediatrics 1994;93:32–6.
[24] Jakaitis BM, Bhatia AM. Definitive peritoneal drainage in the extremely low birth weight infant with spontaneous intestinal perforation: predictors and hospital outcomes. J Perinatol 2015;35:607–11.
[25] Drewett MS, Burge DM. Recurrent neonatal gastro-intestinal problems after spontaneous intestinal perforation. Pediatr Surg Int 2007;23:1081–4.
[26] Holland AJA, Shun A, Martin HCO, et al. Small bowel perforation in the premature neonate: congenital or acquired? Pediatr Surg Int 2003;19:489–94.

[27] Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.

[28] J.L. Aschner, K.S. Deluga, L.A. Metlay, et al. Spontaneous focal gastrointestinal perforation in very low birth weight infants. J Pediatr. 113 (1988) 364–367.

[29] R. Wadhawan, W. Oh, B.R. Vohr, et al. Spontaneous intestinal perforation in extremely low birth weight infants: association with indometacin therapy and effects on neurodevelopmental outcomes at 18-22 months corrected age. Arch Dis Child. Fetal Neonatal Ed. 98 (2013) F127–32.

[30] M. Stavel, J. Wong, Z. Cieslak, et al. Effect of prophylactic indomethacin administration and early feeding on spontaneous intestinal perforation in extremely low-birth-weight infants. J Perinatol. 37 (2017) 188–193.

[31] J.G. Fisher, B.A. Jones, I.M. Gutierrez, et al. Mortality associated with laparotomy-confirmed neonatal spontaneous intestinal perforation: a prospective 5-year multicenter analysis. J Pediatr Surg. 49 (2014) 1215–1219.

[32] R.L. Moss, R.A. Dimmitt, D.C. Barnhart, et al. Laparotomy versus peritoneal drainage for necrotizing enterocolitis and perforation. N Engl J Med. 354 (2006) 2225–2234.

[33] S. Kargl, O. Wagner, W. Pumberger. Ileostomy complications in infants less than 1500 grams — frequent but manageable. J Neonatal Surg. 6 (2017) 4.

[34] Brisighelli G, Consonni D, Macchini F, et al. A single-center experience with very low birth weight infants and focal intestinal perforation: comparison of primary anastomosis versus stoma opening. Eur J Pediatr Surg 2018;5:426–32.

[35] Wallen E, Venkataraman ST, Grosso MJ. et al. Intrahospital transport of critically ill pediatric patients. Crit Care Med 1995:1588–95.

[36] G. Frawley, G. Bayley, P. Chondros. Laparotomy for necrotizing enterocolitis: intensive care nursery compared with operating theatre. J Paediatr Child Health. (1999) 291–5.

[37] Schwebel C, Clec'h C, Magne S, et al. OUTCOMEREA Study Group. Safety of intrahospital transport in ventilated critically ill patients: a multicenter cohort study. Crit Care Med 2013:1919–28.