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Mortality and intestinal failure in surgical necrotizing enterocolitis

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Abstract

Background/Purpose: To examine whether as initial surgical intervention for necrotizing enterocolitis, primary peritoneal drainage as compared to primary laparotomy is associated with increased mortality or intestinal failure.

Methods: Retrospective observational study of 240 infants with surgical necrotizing enterocolitis.

Results: There was no difference concerning the composite outcome of mortality before discharge or survival with intestinal failure after adjusting for known covariates (Odds Ratio 1.73, 95% CI 0.88, 3.40). More surviving infants in the peritoneal drainage with subsequent salvage or secondary laparotomy had intestinal failure compared to those who received a peritoneal drain without subsequent laparotomy and survived (12% vs. 14% vs. 1%, $p=0.015$).

Conclusions: There is no difference between peritoneal drainage and laparotomy in infants with surgical necrotizing enterocolitis concerning the combined outcome of mortality or survival with intestinal failure. There is increased intestinal failure in surviving infants treated with peritoneal drain with either subsequent salvage or secondary laparotomy compared to peritoneal drainage alone.

Necrotizing enterocolitis (NEC) that requires surgical intervention is associated with an overall mortality before discharge of between 40% and 51%. [1,2] Primary peritoneal drainage (PPD) and primary laparotomy are two options for the initial operative management of surgical NEC. Two multicenter randomized controlled trials comparing PPD to primary laparotomy in preterm infants have shown similar mortality for either of these surgical treatments. [3,4] Infants with surgical NEC have worse neurodevelopmental outcomes compared to either medically treated NEC [5] or case–control matched infants without NEC. [1,6] A trial is currently ongoing comparing these surgical treatments with respect to survival without neurodevelopmental impairment. [7] No sufficiently powered prospective randomized clinical trial comparing PPD to laparotomy as initial operations for surgical NEC has addressed the composite outcome of survival with intestinal failure (IF) or mortality before discharge. However a multicenter prospective cohort study has examined the composite outcome of death before discharge or prolonged

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post-operative dependence on parenteral nutrition (PN) (defined as > 85 days of post-operative PN) in 156 extremely low birth weight (ELBW) infants with severe NEC or isolated intestinal perforation (IP) who were initially surgically managed with either peritoneal drainage (n = 80) or laparotomy (n = 76). [8] No statistically significant difference was found between initial drainage versus primary laparotomy in this study (adjusted OR 0.73, 95% CI 0.31–1.74). A multicenter randomized controlled trial has also examined the relative risks of surviving infants with IF, for both PPD and primary laparotomy treatments and stratified by birth weight < 1000 g or ≥ 1000 g. [3] No significant difference was found between the two treatments with regards to the outcome of IF. The trial was not powered to examine the secondary outcome of IF which was defined as dependence on PN at day 90 post-operative status.

There are many definitions of IF or short bowel syndrome (SBS) in the literature including dependence on PN for > 42 days post bowel resection or residual post operative small bowel length < 25% expected for gestational age [9,10] or alive and dependent on PN at day 90 post operative or ≥ 90 days after study enrollment. [11] The composite outcome of mortality before discharge or IF is important as it has many implications for subsequent care including the need for home parenteral nutrition, intestinal rehabilitation, and the concomitant morbidities of central line associated blood stream infections and cholestatic liver disease. [12] There are significant financial costs concerning the management of surviving infants with NEC and IF and the necessary intestinal rehabilitation [13].

The Children's Hospital of Alabama is a hospital with a level IIIC Neonatal Intensive Care Unit that provides neonatal and pediatric surgical care in the southeastern United States. The majority of infants with surgical NEC within this region have been referred to this center for both primary surgical treatment and subsequent intestinal rehabilitation.

Our hypothesis is that PPD is associated with increased mortality before discharge or IF for those surviving to discharge. We performed a retrospective analysis of all infants who underwent surgical treatment at the Children's Hospital of Alabama for NEC during the ten years from 1998 until April 2009. The primary study outcome is a composite outcome of mortality prior to discharge or IF. The definition of IF used is discharge home following initial surgical admission on home parenteral nutrition (PN) for any duration of time.

1. Methods

The hospital's electronic database was searched for all infants who were admitted to the Children's Hospital of Alabama NICU from 1998 until April 2009 with a diagnosis of necrotizing enterocolitis and/or intestinal perforation. The electronic charts of these infants were then examined in detail to ascertain whether at any time during their hospital admission they underwent either laparotomy and/or peritoneal drainage. The electronic clinical notes, operative notes, and where indicated, the paper-based clinical notes were examined in detail to identify those infants with NEC who underwent a surgical procedure. Infants with NEC treated solely by medical methods, infants with isolated intestinal perforations (as diagnosed by operative findings), and those with other gastrointestinal pathologies including malrotation, volvulus, gastroschisis, exomphalos and Meckel's diverticulum were excluded from the study. Infants with major chromosomal and congenital malformations (including congenital heart disease and conjoined twins) were also excluded from the study. Infants who were specifically referred to the Children's Hospital with a diagnosis of confirmed or suspected intestinal stricture (usually suspected from preoperative intestinal contrast studies) were also excluded from the study as these infants underwent surgical laparotomy for a very specific and different surgical indication. A database was created comprising all infants with NEC who underwent either PPD or primary laparotomy as the primary operative treatment.

Both perinatal and surgical treatment variables were examined. The perinatal variables included birth weight, mode of delivery, race, gender, and gestational age in completed weeks, Apgar scores at 1 and 5 min and antenatal corticosteroid administration. Variables pertaining to NEC were recorded including type of first operative procedure performed (PPD or primary laparotomy), whether a salvage or secondary laparotomy was performed following initial PPD, day of life of secondary laparotomy, number of infants who underwent ≥ 2 post drainage laparotomies, number of infants with a subsequent peritoneal drain following initial PPD, and length of hospital stay in days for survivors of either PPD or primary laparotomy. A salvage laparotomy was defined as a laparotomy that occurred within ≤ 7 days and a "secondary laparotomy" as occurring > 7 days following PPD. Mortality outcome was defined as death before discharge. Data concerning PN were collected. IF was defined for the purpose of the study as discharge home following initial surgical admission, on PN for any duration of time.

Statistical analyses were performed using SAS (v.9.2, Cary, NC, USA). Both univariate and multivariable analyses were performed using logistic regression analysis with mortality before discharge or survival with IF as the dependent variable. The independent variables included treatment by either primary laparotomy or PPD. Covariates in the model included birth weight, gestational age in completed weeks, gender, race, 1-min and 5-min Apgar scores, and caesarian delivery (CS). Statistical significance was set with a p value of ≤ 0.05. Institutional Review Board (IRB) approval was obtained for this study including permission to search all electronic databases. Every attempt was made to maintain the anonymous nature of patient data.