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Peritoneal drainage is associated with higher survival rates for necrotizing enterocolitis in premature, extremely low birth weight infants

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ABSTRACT

Background: To evaluate peritoneal drainage (PD) and laparotomy ± resection/ostomy (LAP) as initial approaches to the surgical management of necrotizing enterocolitis (NEC) in premature, extremely low birth weight (ELBW) infants.

Methods: Kids' Inpatient Database (2003-2012) was searched for cases of NEC (*International Classification of Diseases, ninth revision, Clinical Modification* [ICD-9-CM] 777.5x) in premature (<37 weeks), extremely low birth weight (<1000 g) infants. Infants were admitted at <28 days of life. Propensity score (PS)-matched analyses were performed, using end points of hospital mortality, length of stay (LOS), and cost of hospitalization. Cases were matched 1:1 on 48 confounding variables (demographic, clinical, and hospital characteristics and 39 comorbidities).

Results: On PS-matched comparison, PD had higher survival *versus* LAP, $P = 0.0009$. LOS and cost were higher for PD *versus* LAP, $P < 0.003$. Survival rates did not differ between PD + LAP and PD-only treatments. LOS and cost were higher for PD + LAP *versus* PD-only, $P < 0.02$. PD + LAP infants had higher survival *versus* LAP, $P = 0.0193$. LOS and cost were higher for PD + LAP, $P < 0.005$.

Conclusions: A risk-adjusted PS-matched analysis of operative management in premature, ELBW infants with NEC found higher survival rates associated with PD placement *versus* LAP, whether PD was used as definitive treatment or with subsequent LAP even after controlling for potential contributors to selection bias (i.e., stability influencing management preference).

Introduction

Necrotizing enterocolitis (NEC) is a condition with high morbidity and mortality affecting premature infants.[1,2] When NEC is complicated with intestinal perforation and pneumoperitoneum, treatments typically consist of peritoneal drainage (PD), laparotomy (LAP), or PD followed by LAP (PD + LAP). These cases are particularly challenging in

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extremely low birth weight (ELBW) infants (<1000g), as hemodynamic instability and high ventilator settings prevent certain patients from transport to the operating room to undergo LAP with resection. In this setting, some advocate the use of PD as a temporizing measure in preparation for LAP,[3-8] whereas others question its effectiveness in this role.[9-12] Furthermore, the role of PD as a definitive therapy is highly controversial for complicated cases of NEC and has been heavily criticized,[9,13] most recently in a large-scale randomized control trial (RCT).[14] Thus, a consensus is yet to be reached regarding the optimal initial treatment for infants with surgical NEC.

Previous studies describing therapeutic outcomes for surgical NEC have cited selection bias as a potential limitation to fair comparative analyses.[1,15] For example, PD is frequently performed in infants with lower birth weight and gestational age, with additional comorbidities associated with prematurity.[1] Therefore, comparing the surgical approaches against one another while adjusting for comorbid risk has been particularly difficult. To address this issue, two RCTs have been performed; the findings and their interpretations however, have varied significantly[14,16]—a systematic review of RCTs found no conclusive answer as to the optimal choice in initial treatment.[12]

In our study, we sought to compare PD, LAP, and PD + LAP for the treatment of surgical NEC in ELBW infants, whereas controlling for confounding variables that may influence the choice of procedure. By using a propensity score (PS)-matched technique, we were able to account for comorbid risk factors specific to prematurity, including birth weight, gestational age, common congenital anomalies, among others. To date, a large-scale analysis using a national, population-based database examining outcomes of drainage *versus* laparotomy in the treatment of surgical NEC in ELBW infants is yet to be performed. In addition, we compared resource utilization measures between procedure types to determine differences in cost effectiveness between surgical approaches.

Methods

We used the Kids' Inpatient Database (KID) to search for cases of NEC (*International Classification of Diseases, ninth revision, Clinical Modification* [ICD-9-CM] 777.5x) in premature (<37 weeks), extremely low birth weight (<1000 g) infants. The KID is a database sampling national pediatric admissions maintained by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the US Agency for Healthcare Quality and Research, with information on up to 7.6 million weighted cases per year. For this analysis, we used data releases from 2003, 2006, 2009, and 2012. Diagnoses and procedures are coded using the ICD-9-CM. Cases were weighted to project national estimates. All analyses were limited to available data; cases with missing data points were excluded from analyses utilizing the specific variable.

Cases were limited to infants undergoing surgical intervention for NEC, in the form of PD placement (ICD-9-CM 54.91) or LAP (ICD-9-CM 54.0, 54.11, 54.19, as well as procedure codes for bowel resection/ostomy). Definitive PD cases excluded LAP procedures; accordingly, primary LAP procedures excluded PD. Cases in the PD + LAP group were defined as infants undergoing PD followed by LAP, on a subsequent day, as confirmed by the hospital day of procedure. To ensure homogeneity among cases, we analyzed only cases of infants that were admitted at <28 days of life. Cases with disposition coded as "transfer to short term hospital" or "other transfers, including skilled nursing facility, intermediate care, and another type of facility" were excluded from analyses.

Three propensity score (PS)-matched analyses were performed for this study, comparing (1) PD *versus* LAP, (2) PD with subsequent LAP *versus* PD-only, and (3) PD with subsequent LAP *versus* LAP cases. Cases were matched 1:1 using the nearest neighbor method for comparison using 48 confounding variables, such as demographic (calendar year, gender, race, primary payer, and median income quartile) and hospital (bed size, location/teaching status, region, and hospital type). Additional risk-adjustment was performed using a standard set of Elixhauser comorbidities, which include coagulopathy, fluid and electrolyte disorders, among others,[17] and variables associated with prematurity (birth weight, gestational age, and presence of comorbidities—cardiac anomalies, bronchopulmonary dysplasia, intraventricular hemorrhage, respiratory distress syndrome, and multiple gestation), as performed in a previous analysis.[18] End points such as hospital mortality, length of stay (LOS), and cost of hospitalization were compared using the matched cohorts. PS value assignment, case sorting, and matching were performed using *MatchIt*, version 2.4-20 (Cambridge, MA), a supplemental module for *R*, version 2.14.2 (R foundation for Statistical Computing, Vienna, Austria).[19] Cost values were derived from the Cost-to-Charge Ratio values provided by the HCUP[20] and standardized to 2012 US dollars (USD), according to inflation rates provided by the US Bureau of Labor Statistics.[21] We set the significance level at $\alpha = 0.05$, and SPSS Statistics, version 21.0 (IBM, Armonk, NY) was used to analyze data.

This retrospective analysis was deemed to be exempt from full Institutional Review Board review.

Results

Overall, 886 surgical cases were identified, with a 41% survival rate within our unmatched cohort. Primary PD was performed in 384 (47% survival), and primary LAP was performed in 502 (37% survival). Within the PD group, 99 underwent PD + LAP (57% survival), whereas 285 had PD only (43% survival). For a comparison of baseline characteristics in unmatched primary PD *versus* primary LAP cohorts, see Table 1.

A PS-matched comparison was performed between 151 PD and 150 LAP cases. The PD group had higher associated survival (survival OR: 2.25) *versus* LAP, $P = 0.0009$. LOS and cost were higher for PD *versus* LAP, $P < 0.003$. No difference was found in disposition among survivors.

A PS-matched sub analysis was performed between 46 PD + LAP and 45 PD-only cases. Survival rates did not differ between groups. LOS and cost were higher for PD + LAP *versus* PD-only, $P < 0.02$. PD-only had higher rates of disposition to home following hospitalization (OR: 10.8) *versus* PD + LAP, $P = 0.028$.