Surgery-Associated Complications in Necrotizing Enterocolitis: A Multiinstitutional Study

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Purpose: This study was designed to evaluate the wound and stomal complication rate associated with surgical intervention in infants with necrotizing enterocolitis (NEC).

Methods: Comprehensive demographic and perioperative data were collected prospectively from 4 separate university hospitals on 51 infants with surgically treated NEC. The postoperative complication rate included wound (infection, dehiscence) and stomal (prolapse, retraction, necrosis, stricture) problems. For analysis, patients were grouped based on gestational age less than 28 weeks (group I, n = 30) and ≥28 weeks (group II, n = 21). Z-score analysis was used for intergroup evaluation.

Results: Significantly more infants in group I (21 of 30 [70%] versus group II, 6 of 21 [29%]; $P < .001$) were treated initially with Penrose drainage alone, but most eventually underwent laparotomy (group I, 28 of 30 [93%] versus group II, 19 of 21 [91%]; *P* value, not significant). The combined stomal/wound complication rate was significantly higher in group I (14 of 30 [47%]) versus group II (6 of 21 [29%]; $P < .025$). Of 51 patients, one operation was required in 23 (45%), 2 in 18 (35%), 3 in 8 (16%), and 4 in 2 (4%).

Conclusions: Although the stomal/wound complication rate was significantly higher in group I, both groups had very substantial complication rates, emphasizing the vulnerability of this infant population. Parents, especially of very premature babies, should be advised that multiple operations are likely and that complications should be expected.
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INDEX WORDS: Necrotizing enterocolitis, postoperative complications, peritoneal drainage, very low birth weight.

ALTHOUGH THE ETIOLOGY of necrotizing enterocolitis (NEC) is unknown, the association of this disease entity with prematurity remains its strongest clinical correlation. Primarily as a result of improved therapeutic strategies in support of the premature infant, survival of infants with very low birth weight (VLBW) has increased substantially over the past decade, even at very early gestational age. This phenomenon has resulted in a concomitant increase in the need for surgical intervention to treat NEC and intestinal perforation in this population.[1] Furthermore, the mortality rate for babies who undergo surgical intervention for NEC has been shown to be inversely proportional to gestational age at birth and to body weight at the time of surgery.[2-4] Although this observation has been documented in the literature, comparatively little attention has been directed toward the incidence of complications that relate to the surgical intervention per se in very premature infants.

MATERIALS AND METHODS

Investigators representing 4 major university teaching hospitals designed a prospective study to collect and evaluate demographic and perioperative data relating to infants with NEC or intestinal perforation requiring surgical intervention. The institutions included Memorial Hermann Children's Hospital and Lyndon Baines Johnson Hospital (both University of Texas, Houston affiliates), The University of Chicago Children's Hospital, and Texas Children's Hospital. Institutional Review Board approval was obtained according to hospital requirements before initiating the study. Fifty-one infants were entered into the study between July 1998 and July 2000. Infants were divided on the basis of estimated gestational age (EGA) at birth into 2 groups: group I less than 28 weeks EGA and group II ≥ 28 weeks EGA.

In addition to the EGA at birth, the collected data included body weight, age, gender, date of NEC onset, number and type of associated comorbid conditions, date, number, and characteristics of operations performed, operative findings, type and duration of antibiotics used, laboratory values observed, date and number of positive blood cultures and organism type and sensitivity, postoperative complication rate, and in-hospital mortality rate.

Complications included wound infection, dehiscence, herniation, enterocutaneous fistula formation, and stomal problems (including retraction, prolapse, stricture, and necrosis).

Statistical evaluation was carried out using Z-score analysis with statistical significance established on the basis of *P* value less than .05.

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Table 1. Summary of Results

	Group I	Group II	*P* Value†
Patients (no.)	30	21	
Drain (primary)*	21 (70%)	6 (29%)	$<.001$
Laparotomy	28 (93%)	19 (91%)	Not significant
All complications (not including death)	14 (47%)	6 (29%)	$<.025$
All complications (including death)	24 (80%)	11 (52%)	$<.001$

*Drain (primary), peritoneal drainage as the initial operative intervention.

†*P* values based on Z score analysis.

RESULTS

The 51 patients entered into the study had an average EGA of 27.8 weeks (range, 23 to 40 weeks) and an average body weight of 0.712 kg (range, 0.5 to 1.59 kg) for group I and 1.803 kg (range, 0.73 to 3.38 kg) for group II. There were no significant intergroup differences in gender, comorbid conditions, operative findings, positive blood cultures, or antibiotic therapy. However, primary peritoneal drainage was used in 21 of 30 (70%) of group I patients compared with 6 of 21 (29%) in group II ($P < .001$), although the frequency of laparotomies was similar in both groups (93% *v* 91%, respectively; Table 1). The occurrence of enterocutaneous fistulas was higher in group I patients (7 of 30 [23%]) than in group II patients (2 of 21 [10%]; $P < .05$). Furthermore, although there was no significant difference in the rate of any other individual complication (including stomal prolapse, stricture, retraction, necrosis, intraabdominal abscess, wound infection, or wound dehiscence) because of small numbers in each category, the overall complication rate in group I infants (14 of 30 [47%]) was significantly higher than in group II infants (6 of 21 [29%]; $P < .025$). Of 51 patients, one operation was required in 23 (45%), 2 in 18 (35%), 3 in 8 (16%), and 4 in 2 (4%). Finally, the in-hospital mortality rate of 14 of 30 (47%) group I patients was substantially higher than 5 of 21 (24%) group II patients ($P < .01$).

DISCUSSION

The results of this study show a substantial risk of postoperative complication in babies born early in gestation when compared with those born later in gestation. Although these findings may derive, in part, from decreased reserves to sustain an adequate metabolic response to injury,[5,6] they also may result from immature immunologic function in the very premature child. This concept is supported by data that show the mortality rate after surgery for NEC in VLBW infants is largely caused by sepsis. Fungal sepsis in particular is highly lethal.[7] One study reported a catheter-related infection rate of 35% after surgery for NEC.[8] This is a substantially higher infection rate than those normally seen in immunocompetent patient populations. Furthermore, infants ≤30 weeks' gestation with NEC have been reported to have a higher incidence of associated infectious complications after surgical intervention when compared with mature babies.[2]

A third potential factor contributing to postoperative complications after surgery for NEC may be decreased tissue strength in severely premature infants. This phenomenon may account for complications associated with tissue integrity, such as wound dehiscence, anastomotic leakage, and stomal prolapse.[8,9] One study specifically designed to evaluate this issue noted a stoma-related complication rate of 32%, including excessive stomal fluid loss, retraction, and prolapse, in NEC infants.[9]

Several retrospective series outline postoperative complications in some detail in babies with NEC. In one study of babies with a mean birth weight of 1,437 g (range, 510 to 3,742 g) and mean EGA of 30 weeks (range, 22 to 38 weeks), but no group breakdown for analysis based on EGA or birth weight, the complication rate not associated with total parenteral nutrition (TPN) was 54%.[8] In this study, the surgical intervention involved a laparotomy. In a multicenter study in which infants undergoing surgery to treat NEC were grouped according to birth weight and gestational age, there was no significant difference in the complication rate of VLBW premature infants (<1,000 g, ≤27 weeks EGA; 51%) versus heavier, more mature infants (≥1,000 g, >27 weeks EGA; 46%), although there was a significant increase in mortality rate in the VLBW group.[4] The mortality rate was especially high in VLBW infants after laparotomy (82%) versus peritoneal drainage (62%). A third study, evaluating patients with a mean birth weight of 1,350 g and a mean EGA of 29 weeks, reported a lower complication rate of 28% in patients treated initially with peritoneal drainage.[7] This study also did not group patients on the basis of gestational age or birth weight for purposes of analysis, but it does raise an interesting point relative to the potential benefit of peritoneal drainage instead of laparotomy in infants with extensive preexistent underlying injury, limited metabolic reserve, and severe prematurity. In a recent study that evaluated peritoneal drainage versus laparotomy to treat NEC in infants weighing less than 1,000 g, the mortality rate was 58% versus 44%, respectively, but the peritoneal drainage group was substantially sicker on the basis of the clinical data provided.[6] These data suggest that complications might be decreased with the judicious use of peritoneal drainage in severely premature babies with NEC. Unfortunately, there is considerable variability among these and other retrospective studies, both in terms of the parameters/populations evaluated and regarding the often conflicting data generated. As a result,

it is difficult to draw firm conclusions relative to appropriate therapeutic guidelines. This finding supports the use of hypothesis-driven, prospective, controlled clinical trials, which, in contrast to the anecdotal, sometimes sporadic nature of retrospective studies, offer the advantage of evolving more definitive therapeutic conclusions.

The current study shows a high complication rate in severely premature babies undergoing surgical intervention to treat NEC. Whether peritoneal drainage as an initial therapy decreases postoperative complications versus laparotomy remains to be established. Parents, especially of very premature babies, should be advised that multiple operations are likely and that complications should be expected.

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