Necrotizing Enterocolitis in Preterm Infants — Is Laparotomy Necessary?

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The occurrence of intestinal perforation is a catastrophic event at any age. Its occurrence in a very-low-birth-weight infant with necrotizing enterocolitis, however, is particularly hazardous. Unfortunately, the incidence of necrotizing enterocolitis increases with decreasing birth weight. Although necrotizing enterocolitis has many causes, the common pathway leading to intestinal necrosis and perforation is thought to be intestinal ischemia and the invasion of bacteria through an immature mucosal barrier. The resulting perforation, peritonitis, and systemic sepsis occurring in an infant whose health is already tenuous carry a high risk of death and demand prompt intervention.

The standard surgical procedure in such cases has been a laparotomy with resection of all necrotic intestine and intestinal diversion. This approach derives from experience in adults, in whom it would be considered unthinkable to leave necrotic intestine in place. However, laparotomy and resection in very-low-birth-weight infants with necrotizing enterocolitis entail high morbidity and mortality; long-term follow-up shows that good neurodevelopmental outcomes are rare.

Three decades ago, pediatric surgeons, out of desperation, began a bold experiment. Ein and colleagues, in Toronto, reported on a case series of six infants with extremely low birth weights who were treated with a temporizing primary peritoneal-drainage procedure. Three survived, two of whom did not require a second operation. The concept was to relieve the increased intraabdominal pressure, drain the infection, and allow the physiological status of the infants to improve before a definitive operative procedure. This initial report was met with skepticism or even outright hostility from surgical colleagues but was followed in subsequent years by several other small case series, many of which supported a role for primary peritoneal drainage in the treatment of very-low-birth-weight infants. Surprisingly, a substantial number of infants treated with primary peritoneal drainage survived, many without the need for a second operation, although neurodevelopmental outcomes remained poor. Despite its widespread use, the role of primary peritoneal drainage has continued to remain controversial. Even among those who accept the approach, there has been controversy regarding which subgroups of infants are the most likely to benefit. Available data have been limited by bias in the selection of patients, investigator bias in the interpretation of the results, or both.

The study by Moss et al. in this issue of the Journal is a multi-institutional, randomized, controlled trial comparing primary peritoneal drainage with laparotomy and bowel resection for the treatment of intestinal perforation among 117 premature infants with birth weights of less than 1500 g. The primary outcome of the study was survival at 90 days postoperatively, and the secondary outcomes included dependence on parenteral nutrition 90 days postoperatively and length of the hospital stay. No significant differences were observed between the groups in any of these outcomes.

The findings might appear to imply that, since primary peritoneal drainage is a less invasive, simpler, and less costly approach than laparotomy, all infants with birth weights of less than 1500 g who had intestinal perforation should be treated by primary peritoneal drainage. However, before pediatric surgeons, neonatologists, and payers accept that conclusion, the results of this study need to be carefully scrutinized. The study is well designed and is the first to compare the two therapies in similar groups of neonates. That is a noteworthy accomplishment in itself, since randomized, controlled trials of surgical procedures are uncommon and are particularly unusual in pediatric surgery, where most disorders are relatively rare. That said, this study is not the final word on this debate. As discussed by the authors, the study had a power of 77 percent to detect a lowering of the mortality rate from 50 to 25 percent. Thus, differences of less than this magnitude or even of this magnitude could easily have been missed. The power was considerably lower for subgroup analyses. For instance, only 17 infants weighing at least 1000 g were randomly assigned to laparotomy, and 10 to primary peritoneal drainage, which are inadequate numbers from which to draw conclu-
sions. Since these are the infants that most pediatric surgeons would preferentially treat with laparotomy, the inability of this study to provide clear guidance for this group warrants emphasis.

In addition, as the authors acknowledge, the follow-up was insufficient to permit comparison of neurodevelopmental outcomes between the two groups. The importance of long-term follow-up in assessing outcomes is underscored by the results at 18 months of age in a recent multicenter observational study, suggesting a trend, although nonsignificant, toward improved neurodevelopmental outcomes among patients treated with laparotomy, as compared with primary peritoneal drainage.12

Along with the results of their randomized trial, the authors present outcome data for infants who were eligible for but not enrolled in the trial. Among nonenrolled infants, survival at 90 days after laparotomy was 85 percent, far better than that of any other treatment group. The authors reasonably attribute the difference in results between this subgroup and those enrolled in the randomized trial to patient selection and point to these discrepant results as further evidence of the need for a randomized, controlled design. Yet an alternative perspective would be that the excellent outcomes outside the trial reflect what experienced surgeons can achieve by selecting patients whom they consider appropriate for laparotomy.

These limitations notwithstanding, the results strongly support the conclusion that, at least among neonates with birth weights of less than 1000 g, there is no apparent difference in short-term survival, length of hospitalization, or requirement for parenteral nutrition between infants who undergo primary peritoneal drainage and those who undergo laparotomy. These results indicate that primary peritoneal drainage is a reasonable treatment approach in these very tiny patients with tenuous health.

The report by Moss et al. sets a new standard for future studies in this area and should also guide the design of studies of other controversial questions in pediatric surgery. Although this study cannot definitively answer the questions related to primary peritoneal drainage, it provides critical evidence to help guide the decision making of pediatric surgeons and neonatologists as they care for this challenging patient population.

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