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Coming full circle: an evidence-based definition of the timing and type of surgical management of very low-birth-weight (<1000 g) infants with signs of acute intestinal perforation

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Abstract

Objective: Gut disruption in very low birth weight follows 1 of 3 clinical pathways: isolated perforation with sudden free air, metabolic derangement (MD) complicated by appearance of free air, or progressive metabolic deterioration without evidence of free air. To refine evidence-based indications for peritoneal drainage (PD) vs laparotomy (LAP), we hypothesized that MD acuity is the determinant of outcome and should dictate choice of PD or LAP.

Methods: Very low-birth-weight infants referred for surgical care because of free intraperitoneal air or MD associated with signs of enteritis were evaluated by univariate or multivariate logistic regression to investigate the effect on mortality of MD and initial surgical care (LAP vs PD). Metabolic derangement was scaled by assigning 1 point each for thrombocytopenia, metabolic acidosis, neutropenia, left shift of segmented neutrophils, hyponatremia, bacteremia, or hypotension. Laparotomy and PD were stratified by MD acuity, and odds of mortality were calculated for each surgical option.

Results: From October 1991 to December 2003, 65 very low-birth-weight infants with suspected gut disruption were referred for surgical care. Peritoneal drainage and LAP infants had similar birth weight and gastrointestinal age, neither of which predicted mortality. Despite a higher incidence of isolated perforation with sudden free air in PD infants, the incidence of MD and overall mortality were similar for PD and LAP. Multivariate logistic regression demonstrated MD to be the best predictor of mortality (odds ratio [OR], 4.76; confidence interval [CI], 1.41-16.13, $P = .012$), which significantly increased with interval between diagnosis to surgical intervention ($P < .05$). Infants with MD receiving PD had a 4-fold increase in mortality (OR, 4.43; CI, 1.37-14.29; $P = .0126$). Conversely, those without MD and sudden free air who underwent LAP had a 3-fold increase in mortality (OR, 2.915; CI, 1.107-7.692; $P = .03$.) Of 5, 3 failed PD were "rescued" by LAP.

Conclusions: The dramatic difference in mortality odds based on surgical option in the presence of MD defines the critical importance of a thorough assessment of physiological status to exclude MD. Absence of MD warrants consideration for PD, especially for sudden intraperitoneal free air. Overwhelming MD may limit options to PD; however, salvage of 3 of 5 infants with failed PD demonstrates the value of LAP, whenever possible, for infants with MD.

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The increasing sophistication of modern neonatal care has raised the odds of survival for tiny, premature infants [1]. Management of these very low-birth-weight (VLBW) infants commonly involves treatment of multiple organ system dysfunction, often associated with and driven by necrotizing enterocolitis (NEC). Multiple organ insufficiency can produce a level of physiological instability that may essentially eliminate operative intervention as a safe therapeutic alternative for control of catastrophic intra-abdominal infection. In 1977, Ein and colleagues [2], recognizing the increasing incidence of this problem, reported their experience with management of these fragile infants with bedside placement of a peritoneal drainage (PD). As others followed suit, PD began to emerge as an alternative to traditional surgical principles of laparotomy (LAP), debridement, and lavage [3-5]. A metaanalysis of reported experience with surgical management of perforated NEC in VLBW infants (study range, 615-1158 g) suggested that PD was an appropriate alternative for these patients [6]. In 2000, Cass and colleagues [7] reported the irretrospective review of management of VLBW and defined a cohort of infants with sudden appearance of free intraperitoneal air in whom PD was associated with a statistically significant improvement in survival. They postulated that these patients represented a different type of disease process that was best managed by PD alone. Demestre et al [8] evaluated use of PD as initial therapy for both pneumoperitoneum and symptomatic NEC in a 5-year multicentered study. They recommended PD as initial management and emphasized that LAP should only be performed after stabilization. Peritoneal drainage has thus evolved from desperation maneuver for infants too unstable for LAP to definitive treatment of certain VLBW infants [9].

The natural history of gut disruption in VLBW follows 1 of 3 pathways: isolated perforation with sudden free air (SIPA), metabolic derangement (MD) complicated by appearance of free air (MDFA), or progressive metabolic deterioration without evidence of free air (PMD). Timely drainage of the first minimizes peritoneal contamination that will trigger sepsis. Delayed intervention of the last will exacerbate sepsis by allowing its major driver to progress uncontrolled. To refine evidence-based indications for PD vs LAP, we hypothesized that acuity of MD, as the primary determinant of outcome, should dictate the choice of PD or LAP.

1. Methods

The neonatal research database at the University of Florida Health Science Center, Jacksonville, has been accruing clinical patient information continuously since its inception in 1991. Every neonatology patient's data is entered concurrent with care under the supervision of a single neonatologist (RS). The intensive care nursery is a regional perinatal critical care referral facility where a single, multidisciplinary faculty provides care to all admitted babies. With appropriate institutional review board approval, we queried this database for VLBW infants (birth weight [BW] ≤1000 g) referred for surgical care because of free intraperitoneal air or evolving MD as manifested by inability to feed associated with clinical deterioration. The decision to use PD or LAP was made by the attending surgeon. Infants with gestational age (GA) below 23 weeks, congenital anomalies, or chromosomal abnormalities were excluded. To stratify risk within the model, MD was scaled by assigning 1 point each for preintervention presence of abnormal leukocyte or platelet counts, left shift of segmented neutrophils, metabolic acidosis, hyponatremia, hypotension, or bacteremia (Table 1) [10]. The relationship of this acuity scaling system to mortality was tested for the entire study group using Spearman correlation. Univariate and multivariate logistic regression models were used to investigate the effect on mortality of BW, GA, sex, ethnicity, Apgar at 1 and 5 minutes, day of life of perforation, MD, and initial surgical care (LAP vs PD). Infants were then categorized by presence of MD with or without free intraperitoneal air into SIPA (free air, no MD), MDFA (free air and MD), or PMD (no free air and MD). Outcome between initial choice of PD or LAP was then assessed for mortality, mean acuity scale, and odds of mortality for each surgical option.

2. Results

Between October 1991 and December 2003, 65 VLBW infants with suspected gut disruption were referred for surgical care. Exclusion of the 9 babies who received both PD and LAP allowed comparison of 56 infants who received either PD or LAP as initial surgical care. Peritoneal drainage and LAP infants had similar BW and GA (Table 2). Logistic regression demonstrated MD to be the best predictor of mortality, which significantly increased with the time interval from diagnosis to surgical intervention ($P < .05$). Spearman correlation between acuity score (MD) and mortality was highly significant ($P = .0002$; Fig. 1) and demonstrated that mortality was associated with the occurrence of 2 or more findings listed in Table 1.

Table 1 Acuity indicators; list of factors used to define MD before surgical intervention

Thrombocytopenia (platelet count<100 000/mL^3)
Metabolic acidosis (calculated base deficit ≥10 mmol/L)
Neutropenia (absolute neutrophil count <2000/mL^3)
Left shift of segmented neutrophils (≥0.18)
Hyponatremia (serum sodium ≤ 130 mmol/L)
Bacteremia (culture confirmed)
Hypotension (mean arterial blood pressure < adjusted gestational age)