Small Bowel Diameter in Short Bowel Syndrome as a Predictive Factor for Achieving Enteral Autonomy

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Children with short bowel syndrome commonly have dilated small bowel. We found that the extent of dilation was associated with bowel length and that both were related to achieving enteral autonomy. *(J Pediatr 2016;178:275-7).*

The care of patients with short bowel syndrome (SBS) involves challenging decisions concerning the value of further surgical intervention, including transplantation and intestinal-lengthening procedures (ILPs).[1] Although these treatment options can provide benefit, they are not without risk and do not benefit all patients uniformly, making appropriate patient selection critical.[2,3] Prognosis with regard to achieving enteral autonomy in the absence of surgical intervention is one of the most important patient selection factors. Previous research has found percent or residual small bowel length (SBL) to have the strongest effect on patients' odds of achieving enteral autonomy[4-6] and to be a major factor in intestinal adaptation, with greater tissue loss associated with a greater degree of intestinal adaptation.[7,8] This adaptation frequently is accompanied by bowel dilation.[9]

Small bowel dilation (SBD) is a factor that currently is used in the decision to perform an ILP because of the procedure's technical requirements[3,9] but has not been evaluated previously as an independent prognostic factor. Understanding which children develop this type of adaptation may have important implications. The objective of this study was to investigate the prognostic value of SBD and evaluate contributory factors in the progression of SBD in patients with SBS.

Methods

This was a retrospective, single-institution study of pediatric patients with SBS approved by the University of Michigan institutional review board (HUM00063515). Data collected included gestational age, birth weight, age at diagnosis, SBS etiology, SBL, time to reintroduction of enteral nutrition (EN) postresection, presence of an ileocecal valve (ICV), number of bacteremic episodes, history of hyperbilirubinemia, time to enteral autonomy, small bowel transplant or ILP, and SBD. These variables have been suggested previously as prognostic factors in pediatric SBS.[4,5]

SBL was defined per the operative report from the last significant resection performed on each patient. Our center uses a standard method of antimesenteric measurement of unstretched intestine, with lengths recorded from the ligament of Treitz to the ICV or colonic anastomosis. Residual SBL was expressed as a percentage of expected length based on existing data for normal SBL by gestational age.[10] This correction is important, given the rapid bowel growth that occurs during the third trimester. Previous studies, by contrast, have failed to identify uncorrected absolute length as a prognostic factor in SBS.[4,11]

SBD was measured on calibrated luminal contrast studies. Measurements were made perpendicular to the contrast-enhanced margin of the bowel lumen by a board-certified pediatric radiologist (R.S.) with 16 years of experience, and the largest was recorded as the maximum bowel diameter. Measurements >35 mm on lumenal contrast studies were considered dilated bowel because this is similar to a 40-mm flattened intraoperative assessment of diameter, which has been described previously as the minimum diameter required for a successful ILP.[12] Reintroduction of EN was defined as tolerance of at least 24 hours of continuous partial EN postresection. Culture-proven bacteremic episodes before the last measureable luminal contrast study were included. Patients were considered to have a history of hyperbilirubinemia if they had at least 1 total bilirubin measurement >2.5 mg/dL during follow-up. Enteral autonomy was defined as a period of at least 6 months without requiring parenteral nutrition (PN).

Patients with a diagnosis of SBS and adequate imaging to assess SBD at more than 1 time point following bowel resection and before an ILP or achieving enteral autonomy were eligible for inclusion in this study (n = 29). A total of 102 patients in our database were excluded, most of whom did not have adequate imaging available or did not meet our definition of SBS. SBS was defined as dependence on PN for ≥60 days secondary to loss of ≥50% SBL. Patients born

EN	Enteral nutrition
HR	Hazard ratio
ICV	Ileocecal valve
ILP	Intestinal-lengthening procedure
PN	Parenteral nutrition
SBD	Small bowel dilation
SBL	Small bowel length
SBS	Short bowel syndrome

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before the year 2000 were excluded because of the absence of digitally recorded contrast studies. Patients with >1 scan were selected to follow changes in diameter over time for use in time-dependent analysis. Because etiologies of SBS with onset later in life are distinct from neonatal-onset disease, only patients who were diagnosed with SBS in the first 6 weeks of life were included. Luminal contrast studies that demonstrated transient small bowel obstruction or stricture were excluded.

Statistical Analyses

A time-dependent multivariate Cox proportional hazards regression analysis was used to investigate the effect of SBD on time to enteral autonomy. The time variable was defined as the number of days from bowel resection to enteral autonomy, or to the date of last follow-up at which dependence on PN was known (right-censored cases). SBD was represented as a time-dependent covariate based on all scans following bowel resection and before an ILP or enteral autonomy. The event definition was achieving enteral autonomy, so hazard ratios (HRs) indicate the chance, or "hazard," of achieving enteral autonomy. All baseline factors initially were analyzed in a univariate fashion with only covariates found to be significant predictors included in the final model. Multivariate linear regression analysis was used to identify independent predictors of SBD. The final SBD measurement before an ILP or enteral autonomy was the primary outcome variable. All baseline factors were first analyzed in a univariate fashion, and covariates were chosen for the final multivariate model by the use of forward selection.

Results

A total of 29 patients with intestinal failure treated at our institution between 2000 and 2015 met inclusion criteria (**Table I**; available at www.jpeds.com). Average gestational age was 31.7 weeks, and average birth weight was 1.89 kg. Necrotizing enterocolitis was the most common etiology of SBS, and etiologies of SBS were not mutually exclusive, because several patients had more than one of these diagnoses. Sixteen (55%) patients achieved enteral autonomy in an average of 1.3 years, during a mean follow-up of 4.6 years. No patients in this cohort received an intestinal transplant, and 11 patients (38%) underwent ILPs.

Predictors of Enteral Autonomy

Sex, gestational age, birth weight, etiology of SBS, time to reintroduction of EN postresection, presence of an ICV, number of bacteremic episodes, and history of hyperbilirubinemia were not significant predictors of enteral autonomy. Significant predictors of enteral autonomy in univariate analysis included percent SBL (HR = 1.119, $P = .003$) as a baseline covariate and SBD (continuous; HR = 0.936, $P = .013$) as a time-dependent covariate (**Table II**) Using multivariate analysis, we found that neither reached significance despite initial significance in univariate analysis. There appeared to be significant collinearity between the covariates (**Figure**).

Table II. Predictors of enteral autonomy in time-dependent Cox proportional hazards analysis

Univariate analysis of predictors	HR	95% CI	Significance (*P* value)
Male	0.871	0.33-2.33	.783
Gestational age, wk	0.957	0.86-1.07	.421
Birth weight, kg	0.665	0.37-1.20	.179
Etiology*			
Necrotizing enterocolitis	1.437	0.54-3.84	.470
Intestinal atresia	0.454	0.15-1.42	.174
Gastroschisis	0.283	0.06-1.25	.095
Midgut volvulus	0.873	0.25-3.1	.832
% SBL remaining	1.119	1.04-1.21	.003
<10% SBL remaining	0.031	0.00-4.93	.180
ICV present	1.839	0.68-4.98	.231
History of hyperbilirubinemia	0.481	0.16-1.44	.191
Number of bacteremic episodes	0.887	0.73-1.08	.237
Time to reintroduction of EN, d	0.976	0.94-1.02	.220
ILP performed	0.009	0.00-0.56	.026
Small bowel diameter	0.936	0.89-0.99	.013
Multivariate analysis with small bowel diameter			
Small bowel diameter	0.95	0.89-1.02	.150
% SBL	1.07	0.98-1.17	.150

*Etiologies are not mutually exclusive.

Factors Associated with SBD

Sex, gestational age, etiology of SBS, time to reintroduction of EN postresection, presence of an ICV, number of bacteremic episodes, and history of hyperbilirubinemia were not significant predictors of SBD. Diagnoses of intestinal atresia ($P = .051$) and midgut volvulus ($P = .075$), birth weight ($P = .01$), percent SBL ($P < .001$), and <10% SBL remaining ($P = .007$) (**Table III**; available at www.jpeds.com) met forward selection criteria for inclusion in the final model. The final linear regression model included birth weight, percent SBL, diagnosis of intestinal atresia, and diagnosis of midgut volvulus as covariates (**Table III**). Percent SBL (B = −1.06, $P = .001$) and intestinal atresia (B = 11.09, $P = .035$) were both significant predictors of SBD, and birth weight and midgut volvulus were not significant in the multivariate model.

Discussion

We found that larger SBD predicted failure to achieve enteral autonomy, and longer percent SBL predicted successful achievement of enteral autonomy. The identification of SBD as a potential prognostic factor that is associated inversely with the odds of achieving enteral autonomy is a novel finding. When we analyzed these covariates in multivariate analyses, none remained significantly associated with enteral autonomy. This lack of significance is likely due to the collinearity between percent SBL and SBD, as percent SBL was the strongest predictor of SBD in our cohort (**Figure**).

Next, we found that shorter percent SBL and a diagnosis of intestinal atresia were associated with larger SBD in our final multivariate analysis. This identification of intestinal atresia as a factor associated with increased SBD is a novel finding that