



The Outcomes of Treatment in Infants with Short Bowel Syndrome

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J Child Sci 2023;13:e12–e19.

Abstract

Objective We reviewed 50 infant cases with short bowel syndrome (SBS) to examine the treatment outcome of SBS management in a tertiary hospital in Vietnam.

Material and Methods A case series was performed at the National Children's Hospital, Hanoi, Vietnam. A total of 50 cases with SBS were reviewed. Clinical and laboratory characteristics before and after treatment were collected.

Results The most common cause of SBS was necrotizing enterocolitis. Common clinical symptoms included watery stools, dehydration, and malnutrition. After treatment, the patient's weight, albumin, and prothrombin improved markedly. There are 72% of children with good or fair treatment results. The rate of sepsis was high (18%). There was one case with complications of catheter infection and one case of liver failure. Three children died during treatment, one died from septic shock and multiple organ failure, and two died from respiratory failure.

Conclusion This study showed promising treatment outcomes in pediatrics.

Keywords

- ▶ short bowel syndrome
- ▶ clinical
- ▶ subclinical
- ▶ results

Short bowel syndrome (SBS) refers to a malabsorptive condition due to the reduction of more than 75% of small intestine's length, which is under the minimum length for absorbing nutrients and maintaining normal nutritional status. SBS is a serious complication that occurs in infants, which is often caused by conditions such as necrotizing enterocolitis, intestinal atresia, or other conditions that require bowel resection. SBS affects the ability of the intestine to absorb nutrients, losing micronutrients and electrolytes needed for the child's development, thereby delaying the child's development, increasing the risk of abnormal development, causing physical disabilities, and increasing the risk of neonatal mortality if necessary treatment is not provided promptly.^{1,2}

Currently, parenteral nutrition (PN) is one of the fundamental therapeutic approaches in the treatment and management of SBS in neonates.^{3,4} PN has been proven through

previous studies around the world as it is highly effective, has few complications, increases the chances of survival, and improves the quality of life of infants with SBS.^{3,4} However, if using the PN method for a long time, the negative effects of PN on their babies are significant, especially with liver function. Another method used is total parenteral nutrition (TPN), which has also been documented in the literature for its effectiveness in improving child development and nutrient absorption until the babies can be adapted to their existing body condition.⁵ In addition, in cases where the infant is unable to adapt, liver and nerve functions are severely affected, bowel transplantation should be considered.⁵ To optimize the SBS treatment, a multiperspective approach and the participation of clinical experts from a variety of disciplines such as gastrointestinal, surgical, nursing, nutrition, psychology, and social disciplines are required. For each infant with SBS, personalized approaches

received

December 3, 2022

accepted after revision

February 2, 2023

DOI <https://doi.org/>

10.1055/s-0043-1764341.

ISSN 2474-5871.

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Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

are needed to help improve the child's overall condition.^{6,7} To provide evidence about SBS management in a low-middle-income country, we reviewed 50 infant cases with SBS to examine the effectiveness of SBS management in a tertiary hospital in Vietnam.

Materials and Methods

Study Design and Sampling Method

A case series was performed from March 2019 to 2020 on infants who were diagnosed with short bowel syndrome and treated at National Children's Hospital from May 2016 to December 2020. We included all infants diagnosed with short bowel syndrome with at least one of the following criteria²: (1) based on the remaining bowel length after surgery: residual jejunoileal segment ≤ 75 cm for those 1-year old and below or ≤ 100 cm for those aged over 1 year; or (2) based on bowel function after surgery: after small bowel resection, the patient must be fed intravenous support for more than 42 days due to bowel dysfunction. Patients were excluded if (1) patient's family and/or guardians did not allow patients to participate in the study; (2) the medical record was incomplete; and (3) infants with comorbidities requiring long-term PN such as complex congenital heart, chyme pleural effusion, oropharyngeal tumor, etc. Patients were conveniently recruited. During the study period, a total of 50 patients with short bowel syndrome from May 2016 to December 2020 were reviewed. The Institutional Review Board of the National Children's Hospital approved the study protocol (Code: 1424/BVNTW-VNCSKTE).

Study Procedure and Data Collection

The patient was admitted to the hospital and evaluated for clinical and laboratory features before undergoing bowel resection (T_0). After surgery, patients were treated for short bowel syndrome with different regimens based on each patient. Patients were evaluated for clinical and laboratory characteristics before (T_1) and after (T_2) treatment for short bowel syndrome.

In this study, we developed a standardized medical record with all the information required. We then screened and selected patients who matched the inclusion and exclusion criteria. Research team members explained to the patient's caregiver the purpose and significance of the study and asked if the infant could participate in the study. After obtaining the consent of the caregivers, the children were included in the study. We divided the patients who met the study criteria into two groups. For the group of children who were already treated with PN at the hospital, the patient's information was collected into the standardized medical record. In addition, these patients were scheduled for a follow-up visit, or if the child was unable to visit the hospital, the caregiver was called to inquire about the child's current medical condition according to the information in the standardized medical record. For the group of children who participated in the study after starting treatment, we collected information according to standardized medical records through clinical examination and paraclinical tests. Data collectors were

carefully trained to ensure consistent data quality and high accuracy. The collected data were also cross-checked to ensure that the information was not incorrect or missing. The collected data in this study included the following factors.

General Information

Child's medical history: including information on age, gender, obstetric history, birth weight, cause of short bowel syndrome, reason for hospital stay, number of hospital stays, number of surgeries, complications experienced, the length of the remaining bowel from the angle of Treitz, and the status of the ileo-jejunal and colonic valves. Causes of bowel resection were collected from the surgical record, discharge diagnosis, and physical examination. In the study, the main causes of short bowel syndrome in children included necrotizing enterocolitis, megacolon, intestinal atresia, midgut volvulus, and others.

Clinical Symptoms

Nutritional status: The nutritional status of a child was determined by measuring weight and height. Children were weighed with SECA electronic scale. The undernutrition status of children was assessed according to the World Health Organization's standards based on the Z-score threshold compared with the reference population.⁸

$$Z\text{-score} = \frac{\text{Weight measured} - \text{Mean of population reference}}{\text{Standard deviation of population reference}}$$

where

The measured weight was the weight of the patient.

The mean of the reference population was the average weight of children of the same age in Vietnam.

Standard deviation was the standard deviation of the weight of children of the same age in Vietnam.

Malnutrition status of children was divided according to the following levels:

- + No malnutrition: -2 standard deviation (SD)
- + Moderate malnutrition: $-2SD$ to $-3SD$
- + Severe malnutrition: from $-3SD$ to $-4SD$

Water and electrolyte malabsorption and nutritional deficiencies: including information on the number of bowel movements per day, stool characteristics, degree of dehydration, and manifestations of electrolyte disturbances. In addition, children were evaluated for anemia, deficit Vitamin A, Ca and Mg +2, Vitamin D, diarrhea, raw stool, and dehydration.⁹

Infections: including infections such as surgical site infections, catheter infections, and sepsis and other complications if present such as liver failure or osteoporosis

Nutritional status: includes complete or partial PN and enteral nutrition.

Classification of short bowel syndrome: based on the surgical report, surgeon consultation, and clinical examination, including three types: (1) type 1: resection of ileum

with or without ileocecal valve resection; (2) type 2: partial jejunal resection, ileostomy, and terminal jejunal drainage; (3) type 3: mainly jejunal resection, preserving more than 10 cm of terminal ileum and colon.

Laboratory Indicators

Indices to assess the malabsorption of water, electrolytes, and nutrients were collected. Hypokalemia disorder was classified according to three levels: mild (serum potassium concentration from 3 to 3.5 mmol/L); moderate (< 2.5 mmol/L); and severe (< 2 mmol/L).¹⁰ The state of hypomagnesemia was assessed according to two levels: mild (including manifestations such as anorexia, nausea, vomiting, muscle weakness, and asthenia) and severe (including neuromuscular disorders, cardiovascular disorders, metabolic disorders, etc.).¹¹ Blood counts, hemodynamics, and blood biochemistry tests were performed at the time of admission, after surgery, and weekly monitoring during treatment until the patient was discharged, including the hemoglobin (g/L), hematocrit (L/L); prothrombin time (%); international normalized ratio; fibrinogen (g/L); albumin (g/L); sodium, potassium, calcium (g/L); and micronutrients in the blood such as iron, zinc, magnesium, vitamin D, phosphorus (mmol/L). The indicators of complications and infections were also collected, including white blood cell count, neutrophil leukocyte percentage (%), blood infection, wound infection, catheter infection, and liver and kidney function.

Information about Treatment

Child rearing status: information collected includes:

- Complete intravenous nutrition, complete oral nutrition, or combined intravenous and oral nutrition.
- Intravenous feeding route: peripheral vein, central vein, and peripheral vein placed in the center.
- Mean time of intravenous PN nutrition after surgery.
- Time to start oral feeding after small intestine resection.
- Feeding route: oral feeding or feeding pump through the nasogastric tube.

Feeding methods: complete breast milk, fully hydrolyzed milk, combination of breast milk and hydrolyzed milk, and combination of solid food.

Length of hospital stay: calculated in days from the time of admission to the time of discharge, including the length of stay in the hospital for treatment of comorbidities or acquired during treatment.

Information about Treatment Outcomes

We evaluated treatment outcomes according to the following levels (► **Table 1**).

Complications: Complications during treatment were noted, including catheter infection, bacteremia, catheter occlusion, central venous thrombosis, hyperglycemia, micronutrient deficiencies, confusion, and organ dysfunction.

Statistical Analysis

Data were analyzed using SPSS 20.0 software. Descriptive statistics were performed. Paired *t*-test was per-

formed to assess the difference in clinical and laboratory indicators between, before, and after the intervention. Statistical significance was determined with *p*-value < 0.05 .

Results

Of 50 patients, most of them were male (60%) and 6 months old or below (90.0%). SBS mainly in the group of children ≤ 6 months old (90%). The majority of them had SBS due to necrotizing enterocolitis (42.0%), followed by megacolon (22.0%) and intestinal atresia (14.0%). Most of the patients with SBS had type 2 (54.0%) and were in the acute phase (62.0%). Only 40.0 and 34.0% of patients preserved colon and ileocecum valve, respectively. The common clinical symptoms included diarrhea (39.0%), dehydration (30.0%), malnutrition (52.0%), and greasy stool (34.0%). There were 24.0% patients having severe malnutrition. (► **Table 2**)

► **Table 3** shows the laboratory characteristics of patients with SBS before treatment. Vitamin D3 deficit had the highest proportion at 80%, followed by hemoglobin deficit (75.5%), hypoalbuminemia (68.1%), prothrombin deficit (64.3%), and phosphorus deficit (61.5%). Only 12.5% of patients had lack of zinc.

► **Table 4** reveals the characteristics of treatment process. Most of the patients received both enteral nutrition and TPN (96%) approaches. One patient died during treatment. Among the remaining 49 patients, the majority of them received PN through peripheral veins (75.5%), followed by central vein (20.4%). The common nourishing solutions included NaCl 0.9%, ringer, glucose (82.6%), and electrolyte: NaCl 10%, KCl 10% (63.0%), albumin (60.8%) and lipids (39.1%). There were 71.4% of patients receiving oral feeding, and hydrolyzed milk was the primary feeding method (67.3%).

► **Table 5** shows the progress of SBS treatment. The rate of malnutrition reduced from 52 to 36%, and the rate of diarrhea decreased from 78 to 62%. However, these changes were not statistically significant ($p > 0.05$). Only hemoglobin was found to have significant improvement after treatment compared to before treatment ($p < 0.001$). Overall, 26.0% of the patients had good treatment outcomes, 46% had fair outcomes, and 28% had poor outcomes. There were three cases who died after treatment (6.0%). Eighteen percent of patients suffered from sepsis, followed by wound infection at 10%. Weight, red blood cell, prothrombin, albumin, and potassium increased significantly after treatment compared to results before treatment ($p < 0.05$).

Overall, patients mainly had fair treatment outcomes (46%), followed by poor results (28%), and good results (26%). ► **Fig. 1** shows poor treatment outcomes mainly in patients with type 3 short bowel syndrome (47.1%), patients with type 2 short bowel syndrome had fair outcomes (59.3%), and patients with type 1 had good outcomes. However, the difference was not statistically significant with $p > 0.05$.

Table 1 Criteria for evaluating the results of treatment of short bowel syndrome

Criteria	Good	Fair	Poor
Clinical symptom	Children no longer had short bowel syndrome	Patients had mild symptoms after treatment such as less watery stools (3–5 times/d), greasy stools, mild malnutrition.	Patients with severe clinical symptoms after treatment such as moderate or severe malnutrition; diarrhea \geq 6 times/d, with signs of dehydration and electrolyte disturbances
Laboratory results	Laboratory parameters were within normal limits or there was a mild disorder but no clinical manifestations	Laboratory parameters were close to normal and there were no clinical manifestations	Patients with large changes in laboratory parameters suggesting severe anemia, electrolyte disturbances
Nutrition	The patient stopped being dependent on PN and was able to eat and drink independently by mouth completely	The patient was on oral nutrition but partially dependent on the PN	Patients who were completely dependent on PN or must maintain HPN
Complication	No complications or mild complications such as wound infection but stable treatment during treatment	There might be complications during treatment such as sepsis, catheter infection but were treated stably	Patients with severe complications such as unstable sepsis, IFALD, or death
Reoccurrence	The patient did not have to be readmitted because of symptoms of short bowel syndrome	The patient was readmitted after the first postoperative discharge due to severe symptoms of the disease	The patient was readmitted several times after discharge since the first postoperative period due to complications as well as clinical symptoms of short bowel syndrome.

Abbreviations: HPN, home parenteral nutrition; IFALD, intestinal failure-associated liver disease; PN, parenteral nutrition.

Discussion

The study provides some preliminary evidence on the outcome of treatment of short bowel syndrome in infants at a tertiary hospital in Vietnam. The main treatment goals in short bowel syndrome are to maintain the nutritional status of the patient and to normalize the macronutrient and micronutrient status.^{12,13} However, nutritional care for children with the chronic intestinal disease remains a challenge for many pediatricians. Nutritional support for short bowel syndrome patients is complex and must be individualized based on each patient's acute and chronic medical conditions and problems.^{14,15}

The results of the study showed that the percentage of patients with improved clinical and subclinical symptoms before discharge was high. Clinical and laboratory parameters both increased after treatment, especially weight, prothrombin, albumin, and potassium. It indicated that the treatment solved disease symptoms, changed the patient's nutritional status, as well as changed important indicators affecting the metabolism and development of children. Children after treatment could return to normal development. The overall assessment showed that patients mainly had good and fair treatment outcomes, meaning that after treatment, the patient could gradually return to a normal life, and stop receiving PN completely without serious compli-

cations. However, 26% of patients still had a poor treatment outcome, including patients who died, had severe complications after treatment, or had not stopped receiving PN completely and had to be rehospitalized. These patients were mainly patients with short bowel syndrome type 3, who had a large jejunal resection. This is understandable when the jejunum is where most of the nutrients needed for body development are absorbed. Therefore, for these patients, other interventions such as surgical treatment or intestinal transplantation are required to enable the patient to achieve normal growth.

Sepsis and hepatic failure due to intravenous nutrition were the two main causes of death in the majority of studies.^{12,13,16} In this study, there were nine children (18%) with sepsis complications recorded. Sepsis was the cause of death of one child in the study. It was a male child, who underwent surgery for intestinal atresia at 1 day of age, followed by ileostomy and closed drainage 2 weeks later. After this period, the patient's condition did not improve, the child was lethargic, continuously underwent mechanical ventilation and vasopressor therapy, and the body experienced severe infection and toxicity. We supposed that the cause was the anastomotic leaks. On day 6, after surgery to close the ileostomy, the patient died from toxic septic shock and multiple organ failure. We also recorded one case of liver failure due to PN with clinical symptoms including

Table 2 Demographic and clinical characteristics

Characteristic		Frequency (n)	Percentage (%)
Gender (n = 50)	Male	30	60.0
	Female	20	40.0
Age group (n = 50)	≤ 6 mo	45	90.0
	> 6–12 mo	2	4.0
	> 12 mo	3	6.0
Birth history (n = 50)	Full months	35	70.0
	Prematurity	15	30.0
Causes of short bowel syndrome (n = 50)	Necrotizing enterocolitis	21	42.0
	Megacolon	11	22.0
	Intestinal atresia	7	14.0
	Midgut volvulus	8	16.0
	Others	3	6.0
Classification of short bowel syndrome (n = 50)	Type 1	6	12.0
	Type 2	27	54.0
	Type 3	17	34.0
Phases of short bowel syndromes (n = 50)	Acute phase	31	62.0
	Adaptation phase	13	26.0
	Maintenance phase	6	12.0
Condition (n = 50)	Preserved colon	20	40.0
	Preserved ileocecum valve	17	34.0
	None	13	26.0
Clinical symptoms (n = 50)	Malnutrition	26	52.0
	Diarrhea	39	78.0
	Greasy stool	17	34.0
	Signs of dehydration	30	60.0
	Electrolyte disturbances	9	18.0
Malnutrition levels (n = 50)	Not malnutrition ($\geq -2SD$)	24	48.0
	Moderate malnutrition (from $-2SD$ to $-3SD$)	14	28.0
	Severe malnutrition (from $-3SD$ to $-4SD$)	12	24.0

Abbreviations: SD, standard deviation.

progressive jaundice; blood bilirubin and liver enzymes elevated; and albumin and prothrombin decreased. After treatment, the patient returned to normal condition. Another complication was that surgical site infection was still at a high rate (nine patients), which showed that the work of ensuring sterility and postoperative nursing care were not sufficient. Two children died from respiratory failure. This was the result of many causes such as premature birth, poor patient condition and inadequate organ function, malnutrition, infection due to short bowel syndrome, major surgery, and difficult postoperative period. The patient was constantly on a ventilator after surgery and could not remove the endotracheal tube to breathe. The patient eventually developed respiratory failure and died.

The limitation in the treatment of patients with short bowel syndrome in our study was the insufficient medical and surgical treatments. The use of supportive drugs, such as the combination of using trace elements such as iron, zinc, and vitamins intravenously and intestinally, was still limited. We recorded that during the treatment period, only two patients received oral Vitamin A and D. The patient had not undergone procedures to prolong the length of the intestine, making the adaptation process of the remaining bowel more difficult and time-consuming. The nutritional status when discharged from the hospital was not good due to the lack of care and treatment to meet the patient's needs as well as the limited guidance for relatives to take care of the child for treatment at

Table 3 Laboratory characteristics of short bowel syndrome before surgery

Laboratory characteristics		Total	Mean \pm SD	Min	Max	Abnormal condition	
						n	%
Hemoglobin (g/L)		49	124.2 \pm 26.0	61	184	37	75.5
Prothrombin (%)		42	69.9 \pm 22.7	26	117	27	64.3
Electrolyte disturbance	Sodium (mmol/L)	47	136.1 \pm 6.8	120.3	166	23	48.9
	Potassium (mmol/L)	48	4.0 \pm 0.73	2.5	5.4	22	45.8
Albumin (g/L)		47	33.3 \pm 7.3	19.2	51.3	32	68.1
Micronutrient deficiency	Total calcium (mmol/L)	44	2.09 \pm 0.46	0.94	2.75	26	59.1
	Iron (mmol/L)	10	11.17 \pm 8.28	0.2	23.9	4	40.0
	Zinc (mmol/L)	8	15.85 \pm 11.77	7.3	40.98	1	12.5
	Vitamin D3 (mmol/L)	5	30.35 \pm 24.21	16.89	73.34	4	80.0
	Phosphorus (mmol/L)	13	1.28 \pm 0.47	0.58	2.21	8	61.5
	Magnesium (mmol/L)	27	0.72 \pm 0.17	0.44	1.01	9	33.3

Table 4 Treatment characteristics

Characteristics		Frequency (n)	Percentage (%)
Nourishing lines	Enteral nutrition (EN)	1	2.0
	Total parenteral nutrition (TPN)	1	2.0
	Combining EN and TPN	48	96.0
Method of parenteral nutrition	Peripheral veins	37	75.5
	Central vein	10	20.4
	Peripheral inserted central catheter	2	4.1
Nourishing solutions	Albumin	28	60.8
	Lipids	18	39.1
	Red blood cell	17	36.9
	Acid amin	12	23.9
	Infusion: NaCl 0.9%, ringer, glucose	38	82.6
	Electrolyte: NaCl 10%, KCl 10%	29	63.0
	Micronutrient: Mgso4 10%, Cacl ₂ , Vitamin AD	11	23.9
	Vitamin K1	17	36.9
Feeding route	Through the nasogastric tube	14	28.5
	Orally administered	35	71.4
Feeding methods	Breast milk completely	2	4.1
	Hydrolyzed milk completely	33	67.3
	Combined	6	12.2
	Combined with more solid food	8	16.3

home. In addition, the child had not used intravenous feeding with a catheter at home although the remaining intestine was not fully adapted. This caused children to be readmitted to the hospital many times after discharge with repeated diarrhea, dehydration, or malnutrition.

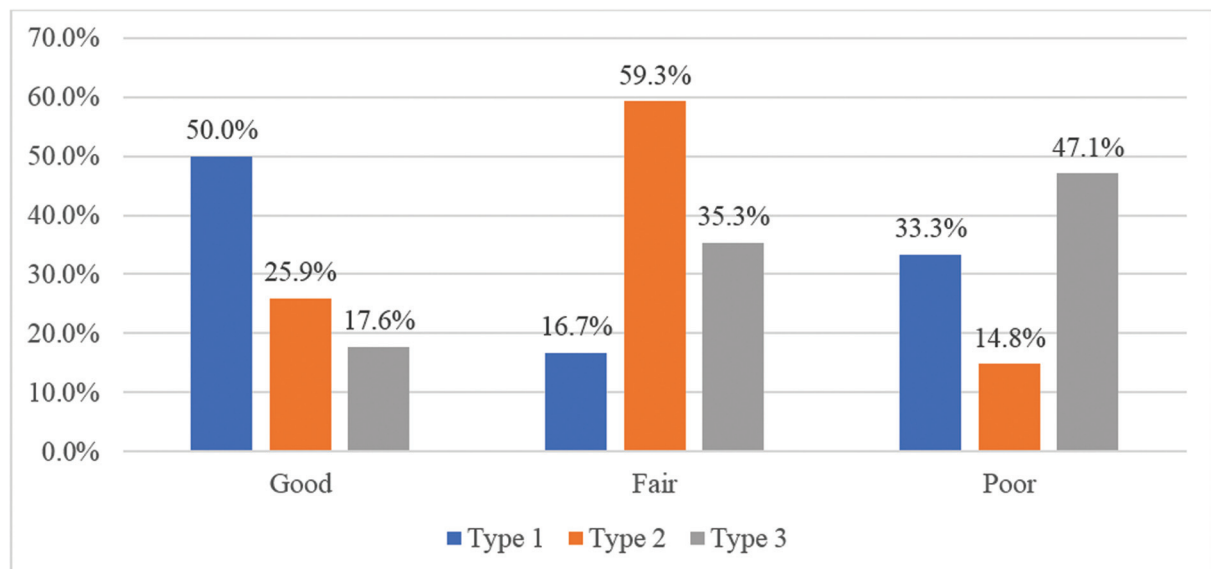
Conclusions

This study showed promising treatment outcomes in pediatric patients with short bowel syndrome. However, problems related to postoperative infection and nutritional status need to be improved.

Table 5 Treatment outcomes

Characteristics	After surgery and before treatment		After treatment		p-Value
	n	%	n	%	
Clinical symptoms					
Malnutrition	26	52.0	18	36.0	0.107
Diarrhea	39	78.0	31	62.0	0.081
Laboratory characteristics					
Deficit Hemoglobin	37	74.0	17	34.0	<0.001
Deficit Prothrombin	27	54.0	19	38.0	0.108
Hypoalbuminemia	32	64.0	23	46.0	0.070
Electrolyte disturbance	27	54.0	18	36.0	0.070
Treatment outcomes					
Good			13	26.0	–
Fair			23	46.0	
Poor			14	28.0	
Complications					
Wound infection			5	10.0	–
Catheter infection			1	2.0	–
Sepsis			9	18.0	–
Intestinal failure-associated liver disease			1	2.0	–
Death			3	6.0	–
	Mean ± SD		Mean ± SD		
Weight (kg)	5.46 ± 2.94		5.68 ± 2.90		0.001
Red blood cell (T/L)	3.58 ± 0.64		3.94 ± 0.81		0.005
Hemoglobin (g/L)	106.47 ± 23.04		113.8 ± 21.83		0.083
Prothrombin (%)	65.54 ± 17.90		78.14 ± 16.60		0.001
Albumin (mmol/L)	30.45 ± 6.43		36.03 ± 7.67		0.001
Sodium (mmol/L)	133.27 ± 8.46		135.88 ± 4.38		0.059
Potassium (mmol/L)	3.68 ± 0.85		4.04 ± 0.69		0.004

Abbreviations: SD, standard deviation.

**Fig. 1** Treatment outcome according to types of short bowel syndrome

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

This study was also approved by The Institutional Review Board of the National Children's Hospital (Code: 1424/BVNTW-VNCSKTE).

Informed Consent

All data were collected anonymously, and patient consent was not required.

Conflict of Interest

None declared.

Acknowledgments

The author is grateful and expresses his thanks to Dr. Toshihiko Watanabe, National Center for Child Health and Development, Division of Surgery (Japan) for giving his advice and time to edit the article.

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