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ORIGINAL RESEARCH

Neonatal intestinal failure: Growth pattern and nutrition intakes in accordance with weaning from parenteral nutrition

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Abstract

Background: Short bowel syndrome is the most common cause of intestinal failure (IF) in infants. We aimed to evaluate growth, nutrition intakes, and predictors of weaning from parenteral nutrition (PN) of infants with IF.

Methods: Clinical parameters, nutrition intakes, body weight and length *z*-scores were compared monthly from the 1st to 12th and at 18 and 24 months among infants receiving PN and those weaned. Logistic regression analysis was conducted to explore the predictors of weaning.

Results: We included 23 infants (10/23 weaned). Median [range: minimum; maximum] birth weight and gestational age were 1620 [590; 3490] g and 31 [24; 39] weeks, respectively. All infants showed growth retardation with similar median delta weight *z*-score from birth to discharge: −1.48 [−1.92; −0.94] in not-weaned and −1.18 [−2.70; 0.31] in weaned infants ($P = 0.833$) and a subsequent regain after the discharge: 0.20 [−3.47; 3.25] and 0.84 [−0.03; 2.58], respectively ($P = 0.518$). No differences in length *z*-score were found. After the sixth month, infants weaned from PN received lower PN energy and protein intakes compared with those not-weaned. Infants weaned from PN showed lower PN dependency index (PNDI%) from 5 months onward (45% for weaned and 113% for not-weaned infants at 5 months: $P < 0.001$). The Belza score, a predictor of enteral autonomy computed at 6 months, is associated with being weaned from PN within 24 months (odds ratio: 1.906; $P = 0.039$).

Conclusion: Infants weaned and not-weaned showed similar growth patterns. Our findings support the clinical relevance of Belza score and PNDI% as predictors of weaning from PN.

KEYWORDS
intestinal failure, growth, parenteral nutrition, predictor of enteral autonomy

CLINICAL RELEVANCY STATEMENT

This study aimed to evaluate growth, nutrition intakes, and predictors of weaning from parenteral nutrition (PN) in infants with intestinal failure (IF) during the first 2 years of life. The growth pattern of infants with IF still receiving PN at 24 months of life was similar to that of weaned infants. Indeed, irrespectively from the PN dependence, all infants showed a postnatal growth retardation during the hospitalization with a following improvement of growth after the discharge. The data obtained in this study showed that the score suggested by Belza et al and the PN dependency index have prognostic relevance on weaning from PN.

BACKGROUND

Intestinal failure (IF) is a rare and complex condition. It is described as a reduction of bowel mass or function below the minimum essential for adequate absorption of nutrients and fluids required for development and survival.[1]

Short bowel syndrome (SBS), resulting from a reduced length of the small intestine, is the most common cause of IF in infants.[2] SBS is a relatively rare disease affecting around 24.5 per 100,000 live births per year,[3] with an incidence inversely related to birth weight.[4,5] Necrotizing enterocolitis (NEC) is the most common cause of SBS in neonates, especially in very low-birth-weight preterm infants, followed by intestinal atresia, gastroschisis, intestinal volvulus, and other less common conditions such as Hirschsprung disease.[3,6] The severity of SBS has been defined in terms of length of residual bowel.

The introduction of parenteral nutrition (PN) has dramatically changed the scenario of infants affected by SBS, not only contributing to improve their survival and growth outcomes but also supporting them until the achievement of enteral autonomy.[7] Nevertheless, dependency from PN is associated with complications that can interfere with growth, such as IF-associated liver disease (IFALD) and central line–associated bloodstream infections (CLABSIs), which are the most fearsome.[2,8,9]

Several authors tried to comprehend the possible factors influencing the achievement of enteral autonomy. Among these factors, the most valuable are the site of resection, the quality and length of residual bowel, the presence of the ileocecal valve, and the length of remaining colon.[10,11]

Recently, Belza et al proposed a SBS disease severity score, which allows providers to predict the probability of achieving enteral autonomy. This score was created according to the following factors evaluated at 6 months postoperatively: small bowel length >50% of estimated small bowel length remaining, the presence of ileocecal valve, conjugated bilirubin <34 μmol/L, and enteral nutrition intakes >50% of total intakes.[12]

In the last years, the calculation of the PN dependency index (PNDI%) as the ratio of nonprotein energy intakes over the resting energy expenditure (REE) was suggested as a predictor of PN dependency rather than the isolated enteral energy, which might be hindered by reduced enteral absorption. It was computed that infants with PNDI% >120% were considered very highly dependent on PN; those with 120%–80% were highly dependent, and those with <80% could be considered moderately dependent.[5,13,14]

The first 2 years after the surgical resection are fundamental for enteral autonomy's achievement of a growing infant.[15] The growth assessment could be a crucial and easily detectable parameter to monitor the nutrition management in healthy infants but even more in vulnerable infants. According to this knowledge, the purpose of this study was to describe the growth pattern of infants with IF during the first 2 years of life and to compare growth and nutrition intakes (parenteral and enteral) of infants still receiving PN at 24 months of life with those infants weaned from PN before the completion of the second year of life. Secondly, possible predictors of weaning from PN in infants with IF have been evaluated.

METHODS

After approval of the study by the Ethical Committee of Fondazione IRCCS (Istituto di Ricovero e Cura a Carattere Scientifico) Ca' Granda Ospedale Maggiore Policlinico, a precise review of the participants' medical records was conducted. Written informed consent was obtained from parents of the infants. The infants included were retrospectively evaluated during their first 24 months of life.

Participants

Infants with IF due to SBS who were admitted into the neonatal intensive care unit (NICU) of the authors' institution and followed by the neonatal nutrition center of the authors' institution, which avails itself of the Intestinal Rehabilitation Program between 2015 and 2019, were included in the present study. IF due to SBS was defined as dependence on PN for at least 90 days after neonatal intestinal resection. Infants affected by congenital or chromosomal abnormalities and neurological disorders, which can interfere with growth and feeding ability, were excluded.

Infants with IF included in the study were categorized as infants weaned from PN within the first 24 months of life and infants still receiving PN at 24 months of life.

Data collection

For each participant, clinical parameters such as sex, birth weight, gestational age (GA), etiology of SBS, clinical history during the first 2 years, including any hospital admissions, duration of hospital stay, duration of fasting, number of surgical interventions, residual intestinal anatomy as length (centimeters), percentage of estimated small bowel length remaining based on GA,[16] and the presence of the colon and ileocecal valve were reviewed.

Time of occurrence of intestinal surgery (days of life and corrected age [CA]), duration of PN dependency, and occurrence of morbidities were also investigated. The CA was calculated using the chronologic age and adjusting for GA, that is, the number of additional weeks from term (40 weeks).[17] In addition, for each infant at 6 months of life, the Belza score[12] was computed.

Nutrition intakes and growth pattern

The nutrition data, including total energy (calories derived by glucose and lipids) and protein intakes, were recorded according to the following timeline: at birth, at surgery, at the first week after surgery (1 week), monthly from the 1st to the 12th months, and at 18 and 24 months of life.

During the hospital stay, nutrition data for enteral and parenteral intakes were extracted from electronic medical records, registered on the software in use in the authors' NICU.

After discharge, parenteral intakes were gathered from medical prescriptions and actual daily infusion. The enteral intakes were derived from a 3-day food questionnaire completed by parents, who were previously instructed for the correct completion of questionnaires, including the type and amount of food, by a member of the nutrition team. Both parenteral energy and protein intakes were recorded in terms of absolute daily intakes (kilocalories per kilogram of body weight per day for energy and grams per kilogram of body weight per day for protein).

The PNDI% was assessed at each study point to evaluate the adequacy of nutrition intakes. The PNDI% is calculated from the ratio between the parenteral energy intake expressed in calories derived from glucose and lipids over the REE expressed as percentage, calculated by using Schofield formula for age, sex, and body weight.[5,18,19]

Body weight and length were recorded at each time point. Corresponding weight and length *z* scores for term infants were calculated using the 2006 World Health Organization (WHO) Growth Standard,[20] whereas the weight and length *z* scores of infants born preterm (GA < 37 weeks) were calculated using the INTERGROWTH-21st tools from birth to 64 weeks' CA.[21–23] The weight and length *z* scores of infants born preterm, after the achievement of 6 months of CA, were calculated using the 2006 WHO Growth Standard, similarly to term infants.

To evaluate the growth during hospital stay and after discharge, delta weight and length *z* scores were computed as differences in *z* scores from birth to discharge and from discharge to 24 months, respectively.

PN weaning process

During hospital stay, weaning from PN was conducted by reducing the daily PN intake in parallel with an increase in the enteral one, with regard to metabolic stability, feeding tolerance, and regular growth until complete weaning has been reached.

After discharge, infants who needed home PN (once they have reached an enteral intake >60% of nutrition requirements, showing stable growth) gradually start PN weaning, according to the Dietary Reference Intake for the Italian Population for specific ages and sex[24] and growth. A gradual reduction of parenteral intakes was introduced by decreasing the time of infusion of PN until the complete weaning, firstly in terms of hours per day and then in terms of numbers of days per week, in accordance with the same criteria observed during the hospital stay (metabolic stability, feeding tolerance, and regular growth).[25]

Discharge criteria of infants with home PN

In those infants who would have needed home PN, a long-term tunneled central venous catheter (CVC) was inserted. When infants were clinically stable and they tolerated enteral nutrition, growing properly, the PN was gradually cycled with an administration, mainly during the overnight period to allow an adequate quality of life at home.

At least two caregivers were trained by the nutrition team of the neonatal nutrition center of the authors' institution to manage the home PN, in aseptic conditions. Infants were discharged in stable conditions, when the caregivers were adequately trained and after a discharge meeting in which the fundamental figures for the optimal management of the patient (a member of our center, the neonatologist and the nurse in charge of caring, a community nurse, a local hospital consultant, and parents) participated.

A specialized nurse and a member of the nutrition team guaranteed a continued helpfulness to support the family at home.

Complications during PN and weaning periods

During the study period, the occurrence of mortality, CLABSI (defined as a positive blood culture), D–lactic acidemia, and IFALD (defined as occurrence of cholestasis: conjugated hyperbilirubinemia associated with conjugated bilirubin >2 mg/dl if the total serum bilirubin is ≤5 mg/dl or >20% of the total serum bilirubin when it is >5 mg/dl)[26,27] were evaluated.

The occurrence of small intestinal bacterial overgrowth (SIBO) was evaluated by the presence of clinical manifestations, such as abdominal distension, bloating, and nausea.

Statistical analysis

Descriptive statistics are presented for all basic characteristics between weaned and not-weaned infants. Continuous variables are presented as median [range] and categorical ones as number (percentage).

Basic characteristics, body weight and length, and the occurrence of morbidities were compared at each time point between infants with IF weaned from PN during the first 24 months and infants still receiving PN. Fisher exact test was used for comparisons of categorical variables, whereas Mann-Whitney *U* test was used for continuous variables. Mann-Whitney *U* test was also used to study the differences in nutrition intakes at each timing and the PNDI% between the two groups. False discovery rate correction was used to adjust the *P* value in this analysis.

Growth overtime was reported using weight and length *z* scores and comparing them between groups using mixed-effect models with subject as random factor.

Finally, logistic regression model was used to study the effect of potential predictors of being weaned from PN within 24 months.

P values <0.05 were considered significant. All analysis were performed using R software version 4.1.2 (R Foundation for Statistical Computing).

RESULTS

Among infants followed by the authors' neonatal nutrition center, 23 infants (14 male infants) who developed IF because of SBS were included in the analysis. Their median weight and GA at birth were 1620 g [range: 590; 3490 g] and 31 weeks [range: 24; 39 weeks], respectively.

During hospitalization, infants underwent a median of three surgical interventions [range: 1; 7] with a consequent interruption of enteral nutrition for a median of 39 days [range: 13; 78 days].

The causes leading to SBS were NEC for 8 (35%) infants, volvulus for 7 (31%) infants, intestinal atresia for 4 (17%) infants, gastroschisis for 3 (13%) infants, and multiple small bowel perforations for 1 (4%) infant.

The median duration of hospital stay was 168 days [range: 55; 396 days]. During the first 2 years of life, 10 (43%) infants were weaned from PN with a median duration of 120 days [range: 98; 600 days] of PN.

In Table 1, basic characteristics of infants weaned and not weaned from PN were described. No differences in basic characteristics at birth, number of surgical interventions, duration of fasting, duration of hospital stay, and in causes leading SBS were detected between the infants weaned from PN and infants not weaned.

Infants weaned from the PN had significantly longer small bowel residual, compared with not-weaned infants; however, they had similar residual colon and presence of ileocecal valve.

Belza score was significantly higher in infants weaned from PN, compared with those not weaned ($P = 0.015$).

Among infants included in the study, 46% of not-weaned infants and 50% of weaned infants had a stoma. Two weaned (15%) and two not-weaned (20%) infants had stoma at discharge. Only one not-weaned infant kept the stoma at 24 months of life (median duration of stoma's maintenance: 3 months [range: 1.5; 18 months] and 5 months [range: 2.5; 24 months], respectively, for weaned and not-weaned infants, [Mann-Whitney *U* test, $P = 0.329$]).

At discharge, all infants included in the study are able to feed orally; the median CA at achieving full oral feeding of infants included was 43 weeks [range: 35; 62 weeks].

After discharge, hospital readmission during the study period was on median equal to 1 [range: 0; 8]. The hospitalization was due to issues related to CVC in the 26% of cases, CLABSI (6.9%), gastroenteritis (23.7%), D-lactic acidosis (4.3%), hematochezia (5%), and to complications not related to SBS (31.5%); these results were similar among the groups.

Among weaned infants, 6 (46%) of them decreased their PN intakes during the hospitalization without cycling the administration of PN. For the other infants, the median age at first cyclization was 104 days [range: 62; 210] vs 77.5 days [range: 60; 210] for infants not weaned from PN and those weaned, respectively.

Nutrition intakes and growth pattern

The absolute actual nutrition intakes (enteral, parenteral, and total intakes) and the comparisons between groups at each time are detailed in Table 2. Infants weaned from PN before completing the second year after surgery received significantly higher enteral intakes, in terms of both energy and protein between 6 and 12 months, compared with not-weaned infants. After 12 months, the not-weaned infants tolerated enteral intakes similar to those of weaned infants.

The PNDI% at each timing according to the study groups are shown in Figure 1. Infants weaned from PN before completing the second year of life showed significantly lower PNDI% from 5 months of life onward. The median PNDI% at 5 months of life was 45% for weaned infants and 113% for not-weaned infants ($P < 0.001$). At the following timings, PNDI% decreases progressively for weaned infants, whereas it remains >90% of REE for not-weaned infants.

The median PNDI% of weaned infants at the time of their suspension of PN was 25.2% (range: 5.6%–42.3%).

The median weight and length *z* scores of infants included in the study and according to study groups are shown in Figure 2. Infants weaned from PN showed similar weight *z* scores throughout the study period (estimate 0.22; $P = 0.323$), compared with the not-weaned infants, during the hospital stay (estimate 0.23; $P = 0.656$) and after the discharge (estimate 0.10; $P = 0.836$). No differences in length *z* scores were detected among groups throughout the study period.

All infants showed a postnatal growth retardation with similar median delta weight *z* score from birth to discharge: −1.48 [−1.92; −0.94] and −1.18 [−2.70; 0.31] in not-weaned and weaned infants, respectively ($P = 0.833$). After discharge, weaned and not-weaned infants had an improvement of growth, irrespective of PN dependence: weight *z* score: 0.20 [−3.47; 3.25] and 0.84 [−0.03; 2.58] in not-weaned and weaned infants, respectively ($P = 0.518$).

Median delta length *z* score during the hospital stay and after discharge reflected the pattern observed for weight *z* score and were similar among groups: −1.23 [−3.10; −0.87] and −1.36 [−5.06; 0.65] in not-weaned and weaned infants, respectively, from birth to discharge ($P = 0.573$) and 0.04 [−2.79; 3.13] and 0.54 [−1.85; 1.72] in not-weaned and weaned infants, respectively, from discharge to 24 months ($P = 0.999$).

Factors associated with weaning from PN

To explore the effect of infants' characteristics on weaning from PN, a logistic regression analysis that included GA, birth weight, presence of colon (partial vs total), and Belza score was conducted (Table 3). The infant who underwent to total resection of the colon was excluded from this analysis. This analysis showed that Belza score is positively associated with being weaned from the PN within 24 months of life (odds ratio: 1.944; $P = 0.031$).

Complications during PN and weaning periods

All the infants survived during the study period. Among the study population, 9 of 10 infants weaned from PN and 2 of 13 not weaned developed IFALD during the hospital stay ($P = 0.317$). After hospital discharge 1 of 10 infants weaned from the PN vs 2 of 13 not-weaned infants developed IFALD ($P = 0.602$). No infants developed portal hypertension during the study period.

TABLE 1 Basic characteristics at time of surgery and residual bowel of infants included in the study

	Not weaned from PN (*n* = 13)	Weaned from PN (*n* = 10)	*P*
Birth weight (g)	1620 [660; 3490]	1673 [590; 3180]	0.832
GA at birth (weeks)	32.3 [26; 39]	30.7 [24; 38]	0.836
Male sex	8 (61.5)	6 (60.0)	0.637
Birth weight *z* score	−0.68 [−0.34; 0.95]	−0.67 [−2.32; 1.1]	0.686
Birth length *z* score	0.24 [−2.18; 1.23]	−0.68 [−2.45; 1.09]	0.898
Age at surgery (days)	5 [1; 22]	10.5 [1; 42]	0.451
CA at surgery (weeks)	34 [26; 39]	33.5 [27; 40]	0.929
Weight at first surgery (g)	1515 [780; 3490]	1673 [930; 3025]	0.878
Surgical interventions (*n*)	3 [1; 7]	2 [2; 6]	0.422
Interruption of EN (days)	40.5 [13; 78]	32 [17; 86]	0.166
Small bowel length (cm)	22 [5; 80]	64 [15; 221]	0.010
Small bowel residual according to GA (%)	18.8 [4.5; 56.3]	41.1 [12; 100]	0.041
Colon			0.410
None: *n* (%)	0 (0)	1 (10)	
Partial	9 (69.3)	5 (50)	
Total	4 (30.7)	4 (40)	
Ileocecal valve	3 (21.4)	4 (40)	0.675
Stoma	6 (46)	5 (50)	0.273
Diagnosis			
NEC	3 (23.1)	5 (50)	
Volvulus	6 (46.2)	1 (10)	
Gastroschisis	1 (7.6)	2 (20)	
Multiple small bowel perforations	0 (0)	1 (10)	
Intestinal atresia	3 (23.1)	1 (10)	
Belza score	2 [2; 7]	5.5 [2; 8]	0.015
Time at discharge (days)	178 [120; 396]	162 [55; 232]	0.442

Note: The data are expressed as median [range] for continuous variables and *n* (%) for categorical variables. *P* values are from *t* test or Mann-Whitney *U* test and Fisher exact test.

Abbreviations: CA, corrected age; GA, gestational age; EN, enteral nutrition; NEC, necrotizing enterocolitis.

No differences in the occurrence of CLABSI (4 of 10 vs 5 of 13 for weaned and not-weaned infants, respectively; $P = 0.789$) emerged between groups. Among infants who had CLABSI, only one developed it after discharge. One infant, weaned from PN, incurred an episode of D-lactic acidemia, associated with clinical SIBO over the study period.

DISCUSSION

This study described the growth pattern and nutrition intakes during the first 2 years of life in 23 infants with IF, secondary to neonatal intestinal resection, according to dependency on PN.

Although most infants included had a birth weight appropriate for GA, they developed a postnatal growth retardation during the hospital stay. The growth retardation observed in our population during hospital stay could be attributed to clinical instability, such as hemodynamic instability and the catabolic state of these infants, during the postsurgical period. In addition, even if these infants received PN during this critical phase, the prolonged fasting and the occurrence of clinical complications could have affected growth.

After the critical phase observed during hospitalization, all the infants showed a subsequent regain of growth. Indeed, the median delta weight and length *z* scores between discharge and 24 months showed an improvement irrespective of PN dependency compared with that

TABLE 2 Nutrition intakes according to study groups

			Not-weaned infants		Weaned infants		
			Median	Range	Median	Range	*P*
V0	Energy (kcal/kg/day)	PN	82.1	74.6; 86.8	78.4	74.2; 92.9	0.723
		EN	0	0; 0	0	0; 0	
		TOT	82.1	74.6; 86.8	78.4	74.2; 92.9	>0.999
	Protein (g/kg/day)	PN	3.4	1.3; 3.8	3.6	2.5; 3.8	0.480
		EN	0	0; 0	0	0; 0	
		TOT	3.4	1.3; 3.8	3.6	2.5; 3.8	0.593
1 month	Energy (kcal/kg/day)	PN	87.5	57.5; 91.3	75.1	67.7; 88.4	0.094
		EN	2.2	0; 17.3	11.5	0; 44.3	0.299
		TOT	89.0	57.6; 108.6	87.9	74.4; 112.0	>0.999
	Protein (g/kg/day)	PN	3.3	2.7; 4.4	3.1	3.0; 3.8	0.318
		EN	0.1	0; 0.6	0.4	0; 1.1	0.480
		TOT	3.7	2.7; 4.8	3.74	3.0; 4.2	0.965
3 months	Energy (kcal/kg/day)	PN	75.4	66.6; 84.7	63.1	8.6; 77.0	0.268
		EN	14.8	0; 84.9	45.7	0; 88.8	0.463
		TOT	88.8	75.4; 120.2	95.2	67.1; 121.3	0.999
	Protein (g/kg/day)	PN	3.0	1.4; 3.8	2.6	0.3; 3.1	0.628
		EN	0.2	0; 3.2	0.8	0; 2.8	0.480
		TOT	3.5	3.0; 3.9	3.5	2.2; 4.0	0.938
6 months	Energy (kcal/kg/day)	PN	61.8	32.0; 76.3	5.1	0; 20.4	0.010
		EN	46.0	14.0; 95.0	116.0	88.3; 170.0	0.004
		TOT	95.4	74.0; 131.0	116.0	88.3; 170.0	0.160
	Protein (g/kg/day)	PN	2.1	1.3; 2.8	0.0	0.0; 2.1	0.018
		EN	0.8	0.2; 3.1	3.0	2.8; 3.7	0.018
		TOT	3.1	2.2; 3.8	3.0	2.8; 3.7	0.938
9 months	Energy (kcal/kg/day)	PN	49.5	25.0; 62.8	0.0	0.0; 48.0	0.074
		EN	55.0	19.8; 88.0	101.4	52.0; 124.0	0.094
		TOT	102.5	68.6; 140.0	104.4	94.0; 124.0	>0.999
	Protein (g/kg/day)	PN	1.9	1.1; 2.7	0.0	0; 2.0	0.114
		EN	1.5	0.6; 2.1	2.1	2.0; 2.9	0.033
		TOT	3.5	2.2; 3.9	2.5	1.9; 4.1	0.514
12 months	Energy (kcal/kg/day)	PN	58.6	20.8; 72.4	0.0	0; 42.0	0.050
		EN	65.0	10.2; 130.0	93.2	74.0; 107.0	0.094
		TOT	114.4	82.6; 160.0	95.0	90.0; 116.0	0.480
	Protein (g/kg/day)	PN	2.1	0.9; 2.6	0.0	0; 1.0	0.023
		EN	1.9	0.3; 2.3	1.9	1.8; 2.9	0.456
		TOT	3.5	2.5; 4.6	2.8	1.8; 2.9	0.028
18 months	Energy (kcal/kg/day)	PN	43.7	27.0; 63.9	0.0	0; 27.0	0.074
		EN	60.0	40.0; 150.0	80.0	65.7; 93.2	0.268
		TOT	103.7	76.5; 152.0	84.8	65.7; 107.0	0.160

(Continues)

TABLE 2 (Continued)

			Not-weaned infants		Weaned infants		
			Median	Range	Median	Range	*P*
	Protein (g/kg/day)	PN	1.6	0.5; 2.4	0.0	0; 0.9	0.045
		EN	2.0	0.9; 2.6	2.2	2.0; 3.0	0.145
		TOT	3.4	2.0; 4.2	2.9	2.0; 3.0	0.051
24 months	Energy (kcal/kg/day)	PN	43.8	19.0; 65.0	0.0	0.0; 0.0	0.010
		EN	80.0	45.0; 126.0	83.5	75.0; 96.0	0.607
		TOT	124.0	90.3; 148.0	83.5	75.0; 96.0	0.012
	Protein (g/kg/day)	PN	1.8	0.5; 2.2	0.0	0.0; 0.0	0.018
		EN	2.1	1; 2.7	2.1	1.7; 2.9	0.960
		TOT	3.6	2.7; 4.5	2.1	1.7; 2.9	0.017

Note: *P* values are from Mann-Whitney *U* test and Fisher exact test.
Abbreviations: EN, enteral nutrition; PN, parenteral nutrition; TOT, total intake; V0, at the time of surgery.

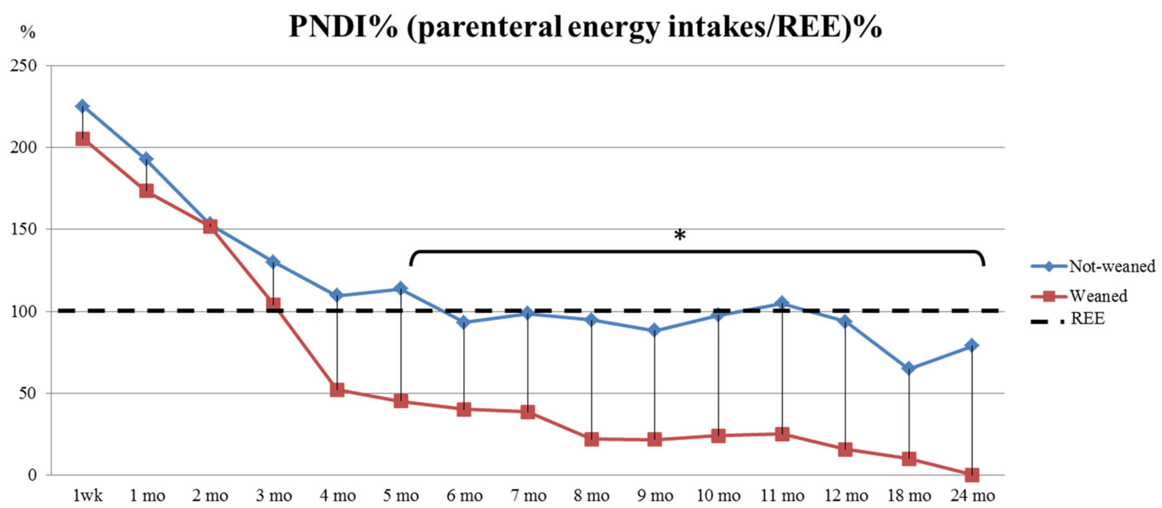

FIGURE 1 PNDI% during the study period. Infants weaned from PN showed lower PNDI% from 5 months onward compared with not-weaned infants. *$P < 0.05$. The analysis was performed by Mann-Whitney *U* test. mo, month; PNDI%, parenteral nutrition dependency index; REE, resting energy expenditure; wk, week.

observed during the hospital stay. These results were consistent with data described by McLaughlin et al,[28] who evaluated the longitudinal growth of a cohort of 41 infants with SBS over the first 2 years of life. They found a growth retardation during the first 6 months, followed by an increase and then a stabilization of the growth pattern.

Our results showed that after 12 months, the not-weaned infants tolerated enteral intake similar to those of weaned infants despite still needing PN. This result could be explained by the smaller residual short bowel length of the not-weaned infants, compared with that of the weaned infants. Consequently, although the not-weaned infants assumed similar enteral intakes compared with the weaned infants, they still needed a quota of the PN to ensure adequate growth because of the lower intestinal absorption than other infants. In fact, as the enteral nutrients could challenge the digestive and absorptive function of the residual bowel, the achievement of weaning off PN was probably facilitated in these infants.

Concerning the PNDI%, weaned infants showed an index of <50% starting from 5 months of life. As suggested by previous studies,[5,18] this could mean that these infants would be on the way to be weaned from PN in the following months.

In our population, the Belza score results associated to being weaned from PN; indeed, for each point of this score, the probability of being weaned within 24 months increases by almost double. In fact, it was significantly higher in infants weaned from PN compared with those not weaned. Belza et al demonstrated that an enteral intake of >50% at 6 months after surgery could be a predictor of the achievement of enteral autonomy (hazard ratio: 5.7 [95% CI: 2.77–11.74]; $P < 0.001$).[12]

It is well known that the presence of residual colon and the remaining ileocecal valve could reduce the duration of PN.[11,29,30] In our population, the presence of colon was not a significant predictor of weaning. This apparent lack of effect could be due to the fact that almost all the infants included had the colon, even if partial.

FIGURE 2 Median weight and length *z* scores during the study period according to weaning from PN (black line). No differences were detected at each timing among groups (dotted lines) both in terms of weight and length *z* scores. Each light blue line refers to a single not-weaned infant. The growth pattern (weight *z* scores) of each weaned infant was outlined with red continuous lines during the period of dependence on PN and in red dotted lines after the PN suspension. mo, month; PN, parenteral nutrition; wk, week.

TABLE 3 Logistic regression analysis

	OR	SE	*P*
GA at birth (weeks)	1.020	0.273	0.941
Birth weight (g)	0.999	0.001	0.715
Belza score	1.944	0.308	0.031
Colon	3.394	1.227	0.319

Note: Basic characteristics and Belza score computed 6 months of life and weaning from PN. Belza score is positively associated with being weaned off PN. Colon: presence of colon (partial vs total).

Abbreviations: GA, gestational age at birth; OR, odds ratio.

In our cohort, we did not find any significant differences in the occurrence of the main complications related to IF between the weaned and not-weaned infants. The occurrence of IFALD was higher during hospital stay, compared with the follow-up period, because of the prolonged fasting related to the surgical intervention and the occurrence of sepsis. After discharge, the reduced occurrence of IFALD could be attributable to infants' stable conditions and to the strategy of administered parenteral lipid 5 times a week, using fish oil–based lipid emulsion (SMOF lipid [0.20 g/ml, Fresenius Kabi]).[31,32] The relative absence of severe complications after the discharge could be due to the adequacy of the follow-up program. Since the early days after surgery, the follow-up program was proposed to all infants by a dedicated team, which comprised several health specialists in gastroenterology, nutrition, pediatrics, surgery, nephrology, radiology, and speech therapy and trained parents.

The lack of measurement of citrulline's values is the main limitation of this study. The evaluations of citrulline's values were performed during the study period, according to the clinical characteristics of each single infant and not complying to a specific timetable; thus, a comparison between the values of each single infant was difficult to perform.

To our knowledge, among all the studies conducted on this topic, this is the first one that describes the growth pattern and nutrition intakes of infants with IF, according to their dependency on PN. In our opinion, more efforts to limit the growth retardation observed during the hospitalization period are desiderable. This period could represent a critical window, being potentially influential on the long-term development of these vulnerable infants.

Regarding the opportunity to achieve enteral autonomy, our findings support the clinical relevance of Belza score and PNDI% as predictors of weaning from PN.

AUTHOR CONTRIBUTIONS

Paola Roggero contributed to the conception and design of the research. Nadia Liotto contributed to the design of the research and drafted the manuscript. Chiara Tabasso, Michela Perrone, Camilla Menis, and Nicola Pesenti contributed to the acquisition and analysis of the data. Paola Piemontese, Anna Orsi, Orsola Amato, Ernesto Leva, and Fabio Mosca contributed to the interpretation of the data. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

CONFLICT OF INTEREST

None declared.

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