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Impact of parenteral nutrition on quality of life, the family and gastrointestinal symptoms in children with intestinal failure

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Abstract

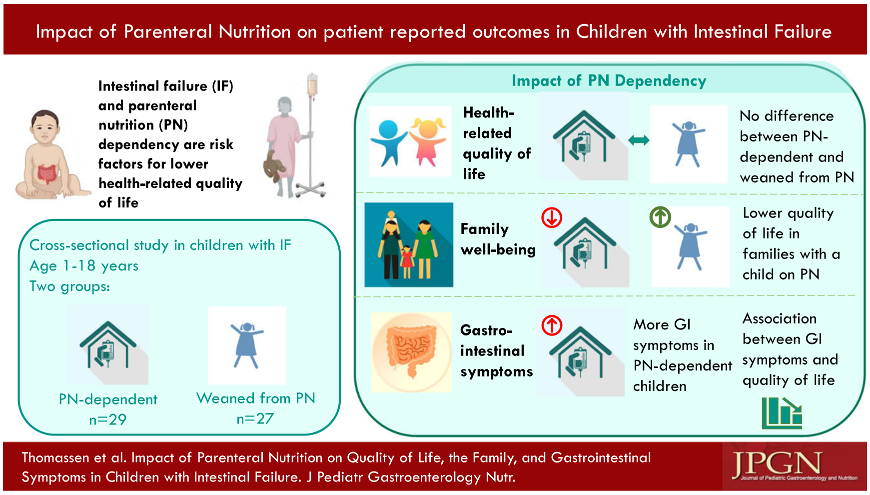
Objectives: Intestinal failure (IF) and dependency on parenteral nutrition (PN) are risk factors for lower health-related quality of life (HRQOL) in children. Weaning from PN is a major goal of paediatric IF treatment, however, its impact on HRQOL remains unclear. This study aimed to assess HRQOL, gastrointestinal (GI) symptoms and family impact in children with IF in relation to their need for PN.

Method: Data were collected in a cross-sectional study from children with IF and a reference group of healthy children using electronic versions of Paediatric Quality of Life Inventory™ forms.

Results: The study included 56 children with IF and 48 healthy children. Parents of children with IF reported significantly lower HRQOL than healthy children (−8.7, $p = 0.001$). PN dependency did not influence HRQOL scores, but families with children dependent on PN had a lower family impact score than children weaned from PN (49.9 vs. 73.6, $p < 0.001$). Parents of children in the PN group reported more GI problems than those in the weaned group (−8.1, $p = 0.04$), and diarrhoea, gas and bloating were common symptoms of IF. GI symptoms varied according to PN dependency and IF aetiology. Multivariate analysis found a significant association between HRQOL and total GI symptom score (parent scores: 0.34, $p = 0.02$, self-score 0.48, $p = 0.02$).

Conclusion: Children with IF had lower parent-reported HRQOL than healthy children. PN dependency did not affect HRQOL, however, the need for PN had a significant negative impact on family well-being. GI symptoms may negatively impact HRQOL in the IF population.

Abbreviations: ASPEN, American Society for Parenteral and Enteral Nutrition; GI, gastrointestinal; HRQOL, health-related quality of life; IF, intestinal failure; PedsQL, Paediatric Quality of Life Inventory; PN, parenteral nutrition; SBS, short bowel syndrome.



KEYWORDS

family impact, health-related quality of life, paediatric intestinal failure, short bowel syndrome, motility disorders

1 | INTRODUCTION

Intestinal failure (IF) is a rare condition characterised by severe intestinal malabsorption, often requiring long-term or lifelong treatment with parenteral nutrition (PN) at home.[1–3] As advances in biomedicine, clinical nutrition and technology have improved survival rates dramatically, the focus has shifted from mere survival to improving the quality of life for these children and their families.[2,4] IF has a significant impact on affected individuals, families and the healthcare system.[5] Children with the condition have a severe disease burden and are at risk for negative long-term effects, such as nutritional deficiencies, impaired bone health and poor growth and development.[3,6–8]

PN is life-saving but carries substantial risks of morbidities, such as PN-induced liver disease and catheter-related complications.[2] Weaning from PN and ensuring good health-related quality of life (HRQOL) are key outcomes in IF treatment,[9] yet little is known about the impact of weaning from PN on HRQOL, gastrointestinal (GI) symptoms and family functioning. Currently, there is no specific module for assessing HRQOL in paediatric patients with IF. Therefore, incorporating measures of GI symptoms is proposed to address this gap.[10] However, the correlation between HRQOL and GI symptoms in paediatric patients with IF remains insufficiently explored.

In this study, we assessed the impact of PN dependency on HRQOL in children with IF and its influence on their families. We further aimed to describe GI symptoms in paediatric patients with IF, taking into account PN dependency, and aetiology. Finally, we analysed the relationship between HRQOL and GI symptoms to determine if including GI symptoms in the assessment could improve the evaluation of HRQOL in paediatric IF.

> **What is Known**
>
> - Weaning from parenteral nutrition (PN) is a treatment goal in paediatric intestinal failure (IF), however, how weaning affects health-related quality of life (HRQOL) is unknown.
> - The association between gastrointestinal (GI) symptoms and HRQOL in children with IF is not well studied.
>
> **What is New**
>
> - PN dependency did not affect HRQOL in children with IF when measured by a generic questionnaire.
> - Children with IF dependent on PN had more GI symptoms than those weaned from PN.
> - GI symptoms were associated with lower quality of life, and including GI symptoms in the assessment could improve the evaluation of HRQOL in children with IF.

2 | METHODS

2.1 | Design and participants

Subjects were recruited to this cross-sectional study in conjunction with recruitment to an ongoing randomised controlled trial in paediatric IF from five paediatric centres in Norway between September 2021 and May 2023 (ClinicalTrials.gov ID: NCT04981262). Patients aged 1–18 years who met the inclusion criteria were invited to participate in the study by written invitation. The inclusion criteria included: diagnosed with congenital malformations or diseases requiring intestinal surgery leading to short bowel syndrome (SBS); diagnosed with severe dysmotility, for example, pseudo-obstruction; or diagnosed with severe enteropathy and need for PN. Additionally, all patients had been treated with PN for a minimum of 60 days within a 74-day period, according to the American Society for Parenteral and Enteral Nutrition (ASPEN) definition of paediatric IF.[1] Children in temporary need of PN due to intercurrent illness, for example, infections, or children with temporary malfunctioning gut due to advanced medical treatment, for example, cancer treatment or transplantation, were excluded.

Data from a healthy reference group collected in a previous study were used for comparison. The participants were recruited by social media and inclusion criteria were residents in the Oslo region, aged 2–18 years, and having a normal diet.[7]

2.2 | Patient characteristics

Information regarding aetiology, prematurity, time of IF diagnosis, comorbidities, surgical procedures, duration of PN, drug therapy and growth were extracted from electronic medical records. Patients were categorised into three groups by aetiology: SBS, motility disorders and other. Nutritional intake and route of administration were obtained from electronic medical records and patient/parent interviews. Patients were categorised into two groups based on their need for PN at the time of the study: on PN or weaned from PN.

2.3 | Outcome variables

Quality of life data were collected using the validated Paediatric Quality of Life Invventory™ (PedsQL™) forms published by Varni et al.[11–13] HRQOL data in the IF and reference group were collected using the PedsQL 4.0 Generic Core Scales, designed to measure core dimensions of health; physical-, emotional-, social- and school functioning, in addition to two multidimensional scores of psychosocial health and total HRQOL. For GI symptoms, the PedsQL™ 3.0 Gastrointestinal Symptom Scales were used. This scale has 10 dimensions of GI symptoms and one multidimensional total score. Family impact data were collected using the PedsQL™ 2.0 Family Impact Module, designed to measure the impact of paediatric chronic health conditions on parents and the family.[13] It consists of six dimensions measuring parent self-reported functioning and two scales measuring family functioning and three multidimensional scores: parent HRQOL, family functioning summary score and total family impact. Parent reports were completed for all age groups, while child/teenage reports were completed by children aged 5 and older. Children 13–24 months were assessed using The PedsQL™ Infant Scales. Permission to use the scoring tools was granted by Mapi Research Trust (http://www.mapi-trust.org/).

The forms were administered electronically or on paper as requested, with questions answered on a 5-point Likert scale (0–4), 0 indicating 'it is never a problem' and 4 'it is almost always a problem'. Each score was then transformed into a 0–100 scale, where 4 = 0 and 0 = 100, with a higher score indicating better quality of life. Scores of healthy children from an earlier cohort study were used for comparison.[7,8] Subgroup analyses based on PN dependency were performed. We hypothesised that children with IF weaned from PN would have a better quality of life compared to those still on PN.

To determine the most common GI symptoms for our patient group, we compared the GI scores of children with IF to cut-off scores in healthy children.[14] Scores equal to or below 1 standard deviation (SD) from the mean of a healthy reference population were considered clinically relevant, indicating symptoms that could negatively impact quality of life.[15] We calculated the proportions of patients with scores meeting this cut-off to assess symptom prevalence.

2.4 | Statistical analysis

Analyses were done in IBM SPSS for Windows, version 29, and STATA 18.0. Mean scores were compared using the independent sample *t*-test and median values were compared using the Mann–Whitney *U*-test based on the distribution of the continuous variable. Cohen *d* was calculated to assess the effect size, that is, the size of the difference between the two groups. An effect size of 0.2–0.49 is considered low, 0.5–0.79 medium and ≥0.8 large.[16] The proportion of GI scores equal to or under 1 SD was compared to the reference group of Varni et al.,[14] and within subgroups of PN dependency and aetiology. Categorical values were compared using Chi-square. For aetiology, scores of children in the category 'other' were excluded due to low numbers. Pearson's correlation and multiple linear regression were performed. The significance level was set to 0.05.

2.5 | Ethics

The study was approved by the Regional Committees for Medical and Health Research Ethics, Norway (REKnr 170851), and by the data protection authorities.

Parents and patients over the age of 16 were asked to consent to participate in the study.

3 | RESULTS

3.1 | Participants

Eighty children diagnosed with IF from five paediatric centres across Norway were invited to participate. Fourteen declined, two were excluded due to language problems and four were unable to participate due to hospitalisation and/or clinical deterioration. There were no differences in age, aetiology, PN treatment or disease severity between the patients not included and those participating in the study. Of the remaining 60 children, 2 failed to complete the quality of life forms and 2 withdrew consent, resulting in 56 children completing the study. Table 1 shows the main characteristics. Approximately half of the children with IF were dependent on PN. There were no significant differences in age, IF diagnosed in infancy, prematurity, underlying diagnosis for surgery, age at resection or gut lengthening procedure between children with IF on PN and weaned from PN. More children were underweight (24% vs. 11%) and stunted (31% vs. 15%) among the PN-dependent children versus those weaned from PN, although the differences were not significant. The weaned group had a higher proportion with SBS ($p = 0.01$) and SBS type 3 ($p = 0.01$). They also had a higher median percentage of remaining small intestine compared to the children on PN ($p = 0.05$). Children in the PN group had been PN-dependent for a median of 6.3 years and were more likely to be on trophic agents like glucagon-like-peptide-2 ($p = 0.01$). Characteristics of the healthy reference group are published elsewhere.[7] The healthy children were older (10.2 vs. 7.9 years, $p = 0.02$), and had a higher proportion of girls included compared to the children with IF ($p = 0.003$).

3.2 | HRQOL

Parents of children with IF reported significantly lower HRQOL scores than parents of healthy children, except for emotional functioning. The effect size ranged from 0.9 to 1.6. There were no significant differences in self-reported HRQOL scores between children with IF and healthy reference groups, with an effect size of 0.1–0.4. In a subgroup analysis of PN dependence, the mean scores of the PN dependent group were lower than the weaned group, however, the differences were not significant (Table 2). Children with motility disorders had significantly lower quality of life than those with SBS (Supporting Information S3: Table 4). Nonsignificant differences were observed among the subtypes of SBS, with parent scores for children with SBS type 1 consistently lower than those with types 2 and 3 (Total HRQOL 67.4 vs. 84.5 and 77.2, respectively, $p = 0.46$).

3.3 | Family impact module

Families with a child dependent on home PN had significantly lower scores in all dimensions of the family impact module than families with children weaned from PN (Figure 1), with an effect size of 0.7–1.3. The mean Family Impact total score was 49.4 (SD 22.9) in families with a child on PN, significantly lower than the score of 73.6 (SD 19.6) in families with a child weaned from PN. Daily activities (30.4 in the PN group vs. 65.7 in the weaned) and parental social functioning (40.6 in the PN group vs. 73.4 in the weaned) were particularly influenced by the need for PN (Supporting Information S2: Table 1).

3.4 | PedsQL Gastrointestinal Symptom Scale scores

The parents of children on PN reported significantly more total GI symptoms and problems with food and drink limits, trouble swallowing, and nausea and vomiting, compared to parents of children weaned from PN, with a corresponding effect size of 0.7–0.8 (Table 3). Children with IF on PN reported significantly more problems with diarrhoea than those weaned from PN, with an effect size of 0.8 (Table 3). More GI symptoms were reported in children with motility disorders compared to SBS and others (Supporting Information S3: Table 5). Minor differences were found in subgroup analysis of SBS type (results not shown).

3.5 | Assessment of the most common GI symptoms

The IF group had a significantly higher proportion of parent-reported GI symptom scores below 1 SD of the healthy reference group for all symptoms except for blood in stools. The symptom with the highest proportion of scores under the cut-off was diarrhoea, followed by gas and bloating (Supporting Information S2: Table 2, Supporting Information S1: Figure 1). Parents of children with IF on PN had a significantly higher proportion of scores under 1 SD for food and drink limits, trouble swallowing, heartburn and reflux, and nausea and vomiting compared to parents of children weaned from PN. A higher proportion of parents of children with motility disorders scored under the cut-off for stomach discomfort when eating and drinking,

TABLE 1 Patient demographics and clinical characteristics.

	Total ($n = 56$)	PN ($n = 29$)	Weaned ($n = 27$)	p Value
Age, years, mean (SD)	7.9 (5.1)	8.6 (5.7)	7.1 (4.7)	0.27[a]
Gender, boys, n (%)	38 (68)	20 (69)	18 (67)	
IF diagnosed in infancy, n (%)	42 (75)	20 (69)	22 (82)	0.22[d]
Prematurity, n (%)	27 (48)	10 (35)	17 (63)	0.06[d]
Moderate/Late (GA 32–37)	13 (23)	4 (14)	9 (33)	
Very preterm (GA 28–32)	1 (2)	1 (3)	0	
Extreme preterm (GA < 28)	13 (23)	5 (17)	8 (30)	
Aetiology, n (%)				0.01[c]
Surgical (SBS)	38 (68)	15 (52)	23 (85)	
Motility	14 (25)	12 (41)	2 (7.5)	
Other	4 (7)	2 (7)	2 (7.5)	
Comorbidities, n (%)				0.11[c]
None	32 (57)	13 (45)	19 (70)	
1–2	15 (27)	9 (31)	6 (22)	
3 or more	9 (16)	7 (24)	2 (8)	
Underlying diagnosis for surgery, n (%)				0.13[c]
NEC	11 (29)	4 (27)	7 (30)	
Midgut volvulus	7 (18)	3 (20)	4 (17)	
Hirschsprung	7 (18)	4 (27)	3 (13)	
Intestinal Atresia	6 (16)	1 (6)	5 (22)	
Abdominal wall defects	6 (16)	3 (20)	3 (13)	
Other surgical	1 (3)	0	1 (4)	
Type of/surgical details of SBS, n (%)				0.01[c]
Type 1	8 (21)	5 (33)	3 (13)	
Type 2	11 (29)	7 (47)	4 (17)	
Type 3	19 (50)	3 (20)	16 (70)	
Age at resection, days, median (range)	5 (1460)	0 (881)	10 (1460)	0.30[b]
% remaining small intestine,[e] median (range)	24% (79)	21% (69)	28% (78,5)	0.05[b]
Gut lengthening, n (%)	7 (18)	3 (20)	4 (17)	0.58[d]
GLP-2, n (%)	11 (29)	8 (53)	3 (13)	0.01[d]
Output Stoma, n (%)	11 (20)	8 (28)	3 (11)	0.18[d]
Nutrition, n (%)				
Feeding tube	28 (50)	19 (65)	9 (33)	0.03[d]
Eating and drinking	50 (89)	25 (86)	25 (93)	0.67[d]
EN	24 (43)	16 (55)	8 (30)	0.06[d]
PN	29 (52)	29 (100)		
Infusions per week, median		7		
PN dependence[f]		60% (34.6)		
Time-dependent on PN (years), median (range)	1.9 (17.7)	5.7 (17.5)	0.6 (7.8)	<0.001[b]

(Continues)

TABLE 1 (Continued)

	Total ($n = 56$)	PN ($n = 29$)	Weaned ($n = 27$)	p Value
Age at weaning from PN (months), median (range)			9.1 (96)	
Growth				
Weight SDS, mean (SD)	−1.01 (1.19)	−1.23 (1.25)	−0.78 (1.09)	0.15[a]
Length SDS, mean (SD)	−0.95 (1.58)	−1.16 (1.64)	−0.73 (1.51)	0.31[a]
BMI SDS, mean (SD)	−0.50 (0.94)	−0.59 (1.08)	−0.40 (0.78)	0.47[a]
Underweight,[g] n (%)	10 (18)	7 (22)	3 (11)	0.18[d]
Stunting,[h] n (%)	13 (23)	9 (31)	4 (15)	0.13[d]
Undernutrition,[i] n (%)	3 (5)	3 (10)	0	0.13[d]

Abbreviations: EN, enteral nutrition; GA, gestational age; GLP-2, glucagon-like-peptide-2; IF, intestinal failure; NEC, necrotising enterocolitis; PN, parenteral nutrition; SBS type 1, end-jejunostomy; SBS type 2, jejunocolic anastomosis; SBS type 3, jejunoileal anastomosis; SBS, short bowel syndrome.

[a]*T*-test.

[b]Mann–Whitney test.

[c]Chi-square.

[d]Fisher's exact test.

[e]Based on values from Strujis et al.

[f]Proportion of estimated energy requirement covered by PN.

[g]Weight ≤ −2SD.

[h]Length ≤ −2SD.

[i]BMI ≤ −2SD.

trouble swallowing, and nausea and vomiting compared to parents of children with SBS.

Diarrhoea emerged as the most frequently reported symptom by the children themselves (Supporting Information S2: Table 2, Supporting Information S1: Figure 1). Heartburn, reflux and diarrhoea were more common symptoms in children with IF on PN compared to children weaned from PN. A higher proportion of children with motility disorders had a total GI symptoms score below the cut-off, and reported gas, bloating and diarrhoea as common symptoms compared to children with SBS.

3.6 | Associations between HRQOL and GI symptoms

A linear regression model showed a significant association between HRQOL and total GI symptom score after correcting for age, PN dependency, aetiology and number of comorbidities (Supporting Information S2: Table 3). Only the number of comorbidities was independently associated with HRQOL.

4 | DISCUSSION

In this study, we found no significant association between PN dependency and generic HRQOL scores in children with IF, however, the families were severely affected by the need for PN. We showed that GI symptoms varied according to PN dependency and aetiology, with more symptoms in children dependent on PN and children with motility disorders. Our analysis revealed an inverse relationship between HRQOL and GI symptoms independent of PN dependency and aetiology.

Our study found significantly lower parent-reported scores for most dimensions of HRQOL in children with IF compared to a healthy reference population. However, the children's own scores did not differ. Previous studies have provided conflicting results on HRQOL in children with IF, some reporting impaired physical functioning and others lower parent scores for emotional, school and psychosocial functioning.[10,17,18] In contrast to our results, two recent studies found lower self-scores in children with IF compared to a healthy reference group in all dimensions of HRQOL.[10,19]

Weaning from PN is a major goal in the treatment of paediatric IF, however, there is limited literature on its impact on HRQOL in this population. Few studies have focused on HRQOL according to PN dependency in children with IF. Lower parent-reported psychosocial health and total HRQOL have been reported in children with IF weaned from PN compared to those on PN.[10] Others have, in contrast, found PN dependency to be associated with lower school functioning.[19] Contrary to our hypothesis, we found no significant differences in HRQOL linked to PN status, whether reported by parents or the children themselves. This suggests that weaning from PN may not improve the child's HRQOL, with other factors like severity of GI symptoms,

TABLE 2 Health-related quality of life: Parent and self-scores for healthy children and children with intestinal failure, including subsets of children with intestinal failure based to their need for parenteral nutrition.

Parent scores		IF			IF versus healthy				PN versus weaned			
Mean (SD)	Healthy ($n = 48$)	Total ($n = 55$)	PN ($n = 28$)	Weaned ($n = 27$)	Diff	95% CI	p Value	Effect size	Diff	95% CI	p Value	Effect size
Total HRQOL	83.7 (10.3)	70.4 (17.2)	66.5 (17.4)	74.4 (16.4)	−13.3	(−18.9 to −7.7)	<0.001	1.3	−7.9	(−17.0–1.2)	0.09	0.5
Psychosocial	81.9 (10.9)	71.4 (16.1)	68.7 (16.1)	74.1 (15.9)	−10.5	(−16.0 to −5.1)	<0.001	1.0	−5.4	(−14.1–3.4)	0.22	0.3
Physical	89.1 (12.2)	69.0 (22.9)	63.2 (24.0)	75.0 (20.4)	−20.1	(−27.4 to −12.7)	<0.001	1.6	−11.8	(−23.8–0.3)	0.06	0.5
Emotional	74.8 (15.8)	72.8 (16.2)	70.0 (16.2)	75.8 (15.9)	−1.9	(−8.2–4.4)	0.63	0.1	−5.7	(−14.4–2.9)	0.19	0.4
Social	88.4 (13.2)	76.4 (21.1)	74.5 (20.7)	78.5 (21.7)	−12.0	(−19.0 to −5.0)	<0.001	0.9	−4.0	(−15.5–7.5)	0.49	0.2
School	82.3 (14.2)	64.8 (22.2)	61.0 (23.5)	68.5 (20.7)	−17.8	(−25.3 to −10.4)	<0.001	1.3	−7.5	(−19.9–5.0)	0.23	0.4
Self-scores		**IF**			**IF versus healthy**				**PN versus weaned**			
Mean (SD)	**Healthy ($n = 47$)**	**Total ($n = 25$)**	**PN ($n = 11$)**	**Weaned ($n = 14$)**	**Diff**	**95% CI**	**p Value**	**Effect size**	**Diff**	**95% CI**	**p Value**	**Effect size**
Total HRQOL	83.0 (10.3)	81.8 (12.0)	79.7 (13.8)	83.5 (10.6)	−1.1	(−6.5–4.3)	0.68	0.1	−3.8	(−13.9–6.3)	0.44	0.4
Psychosocial	80.7 (12.5)	79.1 (13.6)	77.1 (14.7)	80.7 (12.9)	−1.6	(−7.9–4.8)	0.62	0.1	−3.5	(−15.0–7.9)	0.53	0.3
Physical	78.2 (9.7)	85.4 (14.7)	82.7 (18.0)	87.5 (11.8)	−1.9	(−7.6–3.9)	0.66	0.2	−4.8	(−17.2–7.5)	0.43	0.4
Emotional	73.4 (16.8)	78.8 (19.5)	75.5 (18.0)	81.4 (20.2)	5.3	(−3.4–14.0)	0.23	0.3	−6.0	(−20.0–10.1)	0.45	0.3
Social	86.5 (13.8)	83.6 (19.1)	82.7 (13.7)	85.0 (10.7)	−2.5	(−9.4–4.5)	0.48	0.2	−2.3	(−12.4–7.8)	0.65	0.2
School	82.1 (13.2)	77.2 (17.0)	76.4 (16.7)	77.9 (17.7)	−4.9	(−12.1–2.3)	0.18	0.4	−1.5	(−15.8–12.9)	0.83	0.1

Note: Independent sample t-test, Effect size = Cohen's d (standardised mean difference).

Abbreviations: HRQOL, health-related quality of life; IF, intestinal failure; PN, dependent on parenteral nutrition; Weaned, weaned from parenteral nutrition.

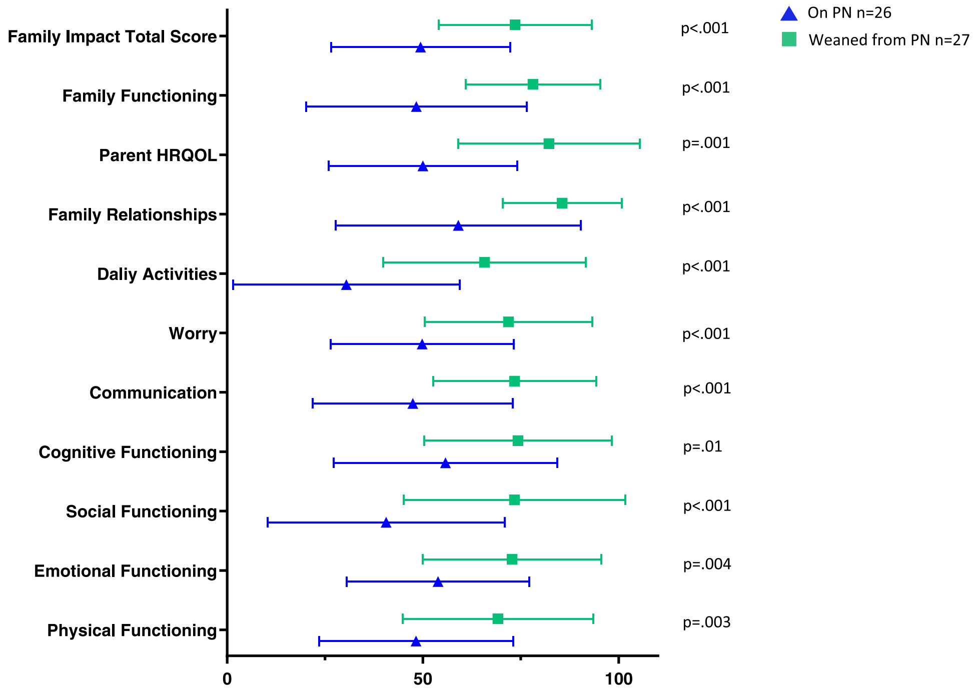


FIGURE 1 Family impact model scores in children with intestinal failure based on their need of parenteral nutrition. HRQOL, health-related quality of life; PN, parenteral nutrition. The triangle denotes the mean value for families with children dependent on parenteral nutrition, while the squares denotes the mean value for families with children weaned from parenteral nutrition. Whiskers represent standard deviation from the mean.

comorbidities and caregiver support having a greater impact than the mode of nutritional therapy. The PN-dependent group included more cases with motility disorders and SBS type 1 compared to the weaned group. This could potentially affect the results since children with motility disorders typically have lower quality of life and more GI symptoms than SBS, and both motility disorders and SBS type 1 have greater difficulty weaning from PN compared to SBS type 3.[20] It is worth noting that both parent- and self-scores of the PN-dependent group were consistently lower than those of the weaned group, indicating that there may be potential differences between the two groups that are not accurately captured by the generic HRQOL forms. In addition, subgroup analysis of SBS subtypes showed no significant differences in HRQOL or GI scores, although trends suggest SBS type 1 could negatively impact quality of life. Specifically, the psychosocial dimensions tended to be affected by the presence of a small bowel stoma. There were also nonsignificant differences in nutritional status, with the PN-dependent being shorter and thinner than the weaned group. The cause of these differences, whether due to underlying disease, management of IF, or nutritional treatment, remains unknown.

While there were no significant differences in HRQOL between children on PN and those weaned from PN, families with a child on PN experienced substantial adverse effects. These families scored significantly lower in all dimensions of the family impact module, with medium to high effect sizes. Previous studies have also found lower quality of life in parents of children with IF and low family impact scores. In one study, PN dependency was linked to lower scores for communication and daily activities.[21] Another study found increased stress, anxiety and depression and lower HRQOL and family impact scores in families with a child reliant on PN compared to healthy.[22] The level of care required for children on PN is substantial, and our study confirms the significant burden placed on parents as daily activity scores in families with PN were particularly low. Caregivers in a previous study reported a median of 29 h per week of direct medical care for their child on PN, emphasising the need for assistance.[23] It is crucial to address these challenges and include psychological support in intestinal rehabilitation teams.

Using generic HRQOL may not fully capture the effects of disease-specific symptoms and challenges related to IF and PN. Unfortunately, there is currently no disease-specific HRQOL module for the paediatric IF population. To address this, it is suggested to incorporate the reporting of GI symptoms alongside generic HRQOLs. However, IF is a heterogeneous condition with various underlying aetiologies and symptoms that may vary greatly among patients. We observed differences in GI symptoms by PN dependency. Children on PN had more GI complaints and experienced more difficulties with GI symptoms related to eating and drinking, and diarrhoea, compared to those weaned from PN. However, there are limited

TABLE 3 Gastrointestinal Symptom Scale: Parent and self-scores for children with intestinal failure, including subsets of children with intestinal failure based on their need for parenteral nutrition.

Parent scores				PN versus weaned			
Mean (SD)	IF ($n = 50$)	PN ($n = 25$)	Weaned ($n = 25$)	Diff	95% CI	p Value	Effect size
Total GI symptom score	70.7 (14.2)	66.3 (12.8)	75.1 (14.4)	−8.8	(−16.5 to −1.0)	0.03	0.6
Stomach pain and hurt	62.6 (23.6)	58.7 (22.4)	66.5 (24.6)	−7.8	(−21.2–5.5)	0.24	0.3
Stomach discomfort when eating and drinking	74.3 (24.3)	71.2 (24.6)	77.4 (24.1)	−6.2	(−20.1–7.7)	0.37	0.3
Food and drink limits	62.7 (33.5)	51.0 (35.4)	74.3 (27.5)	−23.3	(−41.4 to −5.3)	0.01	0.7
Trouble swallowing	86.2 (24.3)	77.0 (28.8)	95.3 (14.2)	−18.3	(−31.3 to −5.4)	0.01	0.8
Heartburn and reflux	81.4 (20.9)	77.5 (16.6)	85.8 (13.9)	−8.3	(−17.0–0.5)	0.06	0.5
Nausea and vomiting	82.4 (20.9)	74.7 (22.8)	90.0 (15.8)	−15.3	(−26.4 to −4.1)	0.01	0.8
Gas and bloating	56.4 (25.1)	54.7 (23.9)	58.1 (26.6)	−3.4	(−17.8–10.9)	0.63	0.1
Constipation	76.5 (17.9)	77.0 (15.3)	76.1 (20.1)	0.8	(−10.2–11.9)	0.88	0.0
Blood in stool	95.0 (11.6)	96.5 (6.8)	93.5 (14.9)	3.0	(−3.6–9.6)	0.37	0.4
Diarrhoea	65.1 (11.6)	66.3 (22.9)	75.1 (14.4)	−8.6	(−21.1–3.8)	0.17	0.7
Self-scores				**PN versus weaned**			
Mean (SD)	**IF ($n = 24$)**	**PN ($n = 11$)**	**Weaned ($n = 13$)**	**Diff**	**95% CI**	**p Value**	**Effect size**
Total GI symptom score	81.0 (12.1)	79.1 (11.7)	81.3 (13.5)	−2.2	(−13.0–8.6)	0.68	0.2
Stomach pain and hurt	76.6 (21.9)	81.1 (20.1)	72.8 (23.5)	8.3	(−10.4–27.0)	0.37	0.4
Stomach discomfort when eating and drinking	85.4 (18.5)	88.6 (15.3)	82.7 (21.0)	5.9	(−9.9–21.8)	0.44	0.3
Food and drink limits	72.6 (31.0)	64.8 (41.8)	79.2 (16.9)	−14.4	(−40.6–11.8)	0.27	0.5
Trouble swallowing	95.5 (10.0)	95.5 (10.8)	95.5 (10.0)	−0.1	(−8.5–8.7)	0.99	0.0
Heartburn and reflux	86.2 (14.4)	81.3 (15.8)	90.4 (12.1)	−9.1	(−21.0–2.7)	0.12	0.6
Nausea and vomiting	91.4 (14.8)	89.8 (19.8)	92.8 (9.5)	−3.0	(−15.8–9.8)	0.63	0.2
Gas and bloating	69.2 (24.8)	68.8 (24.3)	69.5 (26.1)	−0.7	(−22.2–20.9)	0.95	0.0
Constipation	81.8 (14.6)	80.2 (16.4)	82.0 (13.4)	−1.8	(15.9–12.3)	0.79	0.1
Blood in stool	97.9 (6.0)	97.7 (7.5)	98.1 (4.7)	−0.3	(−5.6–4.9)	0.89	0.1
Diarrhoea	72.6 (21.4)	63.3 (22.8)	80.3 (13.5)	−17.2	(−34.1 to −0.3)	0.05	0.8

Note: Independent sample *t*-test, Effect size = Cohen's *d* (standardised mean difference).

Abbreviations: GI, gastrointestinal; IF, intestinal failure; PN, dependent on parenteral nutrition; Weaned, weaned from parenteral nutrition.

studies on the association between GI symptoms and PN dependency in patients with IF. One study reported lower total GI symptom scores in children with IF compared to healthy children, with no reference to PN status. Another study reported a high frequency of loose stools in children weaned from PN.[9,10]

Reporting the mean score for one symptom alone does not provide insight into how many patients experience that particular symptom. To pinpoint the most frequent symptoms for our paediatric IF population, we identified symptoms with a high proportion of children scoring equal to or below the cut-off of 1 SD of a healthy population.[14] This is the first study to report such scores in a paediatric IF population. Our findings indicate that a considerable proportion of children with IF experience gas, bloating and diarrhoea, suggesting that these are common symptoms of IF. Symptoms linked to oral intake of food and drink, as well as tolerance for enteral nutrition (e.g., reflux and vomiting), were, as expected, more frequent in children receiving PN. Furthermore, common symptoms varied based on the underlying causes of IF.

The present study found an association between HRQOL and total GI score, which remained significant after adjusting for age, PN dependency, aetiology and a number of comorbidities. In a multivariate analysis, only the number of comorbidities was independently associated with HRQOL. Previous studies have shown that GI symptoms, such as abdominal pain, loose stools and eating problems, are linked to HRQOL in adults with IF, while diarrhoea has been found to reduce HRQOL in toddlers with IF.[17,24] Similarly, in children with IF stool frequency, loose stools and abdominal pain have been linked to lower HRQOL.[17] While the GI symptom scale may be a useful tool for assessing HRQOL in children with IF, constipation accounts for 25% of the total GI score, which may skew the overall assessment. Given that constipation was not common in our cohort of children with IF, the total GI score might not accurately reflect their quality of life. Therefore, further studies are needed to investigate the relationship between HRQOL and GI symptoms in paediatric IF. Moreover, the GI symptom scale does not address the challenges of PN dependency. Hence, there is a need to develop a disease-specific quality-of-life tool that incorporates common challenges in children with IF, such as relevant GI symptoms, sleep, fatigue and dependence on PN, among other factors. Other authors have advocated for disease-specific questionnaires to better understand how the condition affects the HRQOL in paediatric patients.[17]

While weaning from PN is crucial for reducing morbidity, and mortality, children with IF weaned from PN in this study did not show improved HRQOL compared to those dependent on PN. However, they had higher total GI symptom scores, that is, fewer GI symptoms, which indicates better quality of life. Nevertheless, the parents of PN-dependent children may compensate for the limitations imposed by PN, thereby limiting its impact on the child's HRQOL. Moreover, transitioning into adulthood may further worsen the HRQOL of the IF patients on PN as they become more self-dependent. As weaning from PN is a major goal, health professionals working with paediatric IF should be aware of the apparent limited effect of weaning on the child's HRQOL. Regular follow-up should continue after weaning from PN as these children still have health issues affecting their quality of life. Assessing and following GI symptoms using standardised forms could enhance the quality of care for this patient group and may give a better indication of how the disease affects the quality of life than generic HRQOL forms. Measuring HRQOL and GI symptoms before and after patients are weaned from PN may give more insight into how PN affects children with IF and should be the focus of future studies. More research into how PN affects various aspects of life in children with IF, for example, sleep, fatigue and child/parent relationship, as well as the link between GI symptoms and HRQOL in paediatric IF is needed to further improve the treatment of this patient group.

There are some limitations of this study. The relatively small sample size of children with IF imposes a need for caution when interpreting subgroup analysis results. The heterogeneous nature of IF makes it difficult to make assumptions for this group of patients. Despite our efforts to include all patients in Norway with IF, the rarity of the condition limit the power, which in turn could lead to type 2 errors and failure to identify significant differences. The data are collected in a cohort from Norway, and results may not be representative of the IF population in countries with different economies and health systems. Collecting data on HRQOL in children is challenging. Child self-report depends on the child's developmental state, environment, timing and current disease state, among others. Child and parent by proxy reports do not always agree, especially as the children become teenagers. By proxy, scores will also be influenced by factors within the parents themselves. These factors influence the reliability of our study. To compensate for these challenges, we collected both self- and by-proxy reports, as well as family quality of life, as recommended in the literature.[25]

In conclusion, paediatric patients with IF had a lower parent-reported HRQOL compared to a healthy reference group, although there were no differences in the children's own scores. PN dependency did not seem to affect the patient's HRQOL but had a significant impact on the family. Subgroup analysis showed differences in GI scores, with gas, bloating and diarrhoea being the most common symptoms of IF. HRQOL scores were associated with GI symptom scores, suggesting that including GI symptoms in the assessment could improve the evaluation of HRQOL in children with IF.

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CONFLICT OF INTEREST STATEMENT

Rut Anne Thomassen and Dr. Anne Charlotte Brun have participated as consultants and speakers for Takeda. The remaining authors declare no conflict of interest.

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REFERENCES

1. Modi BP, Galloway DP, Gura K, et al. ASPEN definitions in pediatric intestinal failure. *J Parenter Enter Nutr*. 2022;46(1):42-59.
2. Gosselin KB, Duggan C. Enteral nutrition in the management of pediatric intestinal failure. *J Pediatr*. 2014;165(6):1085-1090.
3. Lezo A, Diamanti A, Marinier EM, et al. Chronic intestinal failure in children: an international multicenter cross-sectional survey. *Nutrients*. 2022;14(9):1889.
4. Varni JW, Limbers CA, Burwinkle TM. Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. *Health Qual Life Outcomes*. 2007;5:43.
5. Allan P, Lal S. Intestinal failure: a review. *F1000Research*. 2018;7:85.
6. Vlug LE, Legerstee JS, Tabbers MM, et al. Children with intestinal failure are at risk for psychopathology and trauma. *J Pediatr Gastroenterol Nutr*. 2023;77(6):e104-e113.
7. Thomassen RA, Kvammen JA, Sæland C, et al. Micronutrients in paediatric intestinal failure patients receiving home parenteral nutrition. *Clin Nutr*. 2020;39:3452-3460.
8. Kvammen JA, Thomassen RA, Kjeserud CN, et al. Bone mineral density and vitamin D in paediatric intestinal failure patients receiving home parenteral nutrition. *Clin Nutr ESPEN*. 2020;39:234-241.
9. Mutanen A, Kosola S, Merras-Salmio L, Kolho KL, Pakarinen MP. Long-term health-related quality of life of patients with pediatric onset intestinal failure. *J Pediatr Surg*. 2015;50(11):1854-1858.
10. McCaig JK, Henry OS, Stamm DA, et al. Generic and disease-specific health-related quality of life in pediatric intestinal failure. *J Pediatr Gastroenterol Nutr*. 2021;73(3):338-344.
11. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care*. 2001;39(8):800-812.
12. Varni JW, Kay MT, Limbers CA, Franciosi JP, Pohl JF. PedsQL gastrointestinal symptoms module item development: qualitative methods. *J Pediatr Gastroenterol Nutr*. 2012;54(5):664-671.
13. Varni JW, Sherman SA, Burwinkle TM, Dickinson PE, Dixon P. The PedsQL™ family impact module: preliminary reliability and validity. *Health Qual Life Outcomes*. 2004;2(1):55.
14. Varni JW, Bendo CB, Shulman RJ, et al. Interpretability of the PedsQL™ gastrointestinal symptoms scales and gastrointestinal worry scales in pediatric patients with functional and organic gastrointestinal diseases. *J Pediatr Psychol*. 2015;40(6):591-601.
15. Splinter A, Tjaden LA, Haverman L, et al. Children on dialysis as well as renal transplanted children report severely impaired health-related quality of life. *Qual Life Res*. 2018;27(6):1445-1454.
16. Sullivan GM, Feinn R. Using effect size—or why the P value is not enough. *J Grad Med Educ*. 2012;4(3):279-282.
17. Hukkinen M, Merras-Salmio L, Pakarinen MP. Health-related quality of life and neurodevelopmental outcomes among children with intestinal failure. *Semin Pediatr Surg*. 2018;27(4):273-279.
18. Neam VC, Oron AP, Nair D, Edwards T, Horslen SP, Javid PJ. Factors associated with health-related quality of life in children with intestinal failure. *J Pediatr*. 2020;216:13-18.e1.
19. Wong M, Neam VC, Horslen SP, Faino A, Javid PJ. Child self-reported quality of life in pediatric intestinal failure. *J Pediatr Surg*. 2022;57(9):143-148.
20. Tappenden KA. Pathophysiology of short bowel syndrome: considerations of resected and residual anatomy. *J Parenter Enter Nutr*. 2014;38(1 suppl):14S-22S.
21. Neam VC, Faino A, O'Hara M, Wendel D, Horslen SP, Javid PJ. Prospective evaluation of the family's health-related quality of life in pediatric intestinal failure. *J Parenter Enter Nutr*. 2022;46(3):652-659.
22. Belza C, Avitzur Y, Ungar WJ, Stremler R, Fehlings D, Wales PW. Stress, anxiety, depression, and health-related quality of life in caregivers of children with intestinal failure receiving parenteral nutrition: a cross-sectional survey study. *J Parenter Enter Nutr*. 2023;47(3):342-353.
23. Belza C, Ungar WJ, Avitzur Y, Stremler R, Fehlings D, Wales PW. Carrying the burden: informal care requirements by caregivers of children with intestinal failure receiving home parenteral nutrition. *J Pediatr*. 2022;250:75-82.e3.
24. Sanchez SE, McAteer JP, Goldin AB, Horslen S, Huebner CE, Javid PJ. Health-related quality of life in children with intestinal failure. *J Pediatr Gastroenterol Nutr*. 2013;57(3):330-334.
25. Lamparyk K, Burkhart K, Buzenski J, van Tilburg MAL. Challenges and opportunities in measuring the pediatric quality of life: exemplified by research in pediatric gastroenterology. *Expert Rev Pharmacoecon Outcomes Res*. 2021;21(2):211-219.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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