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Nutritional status in children with cancer

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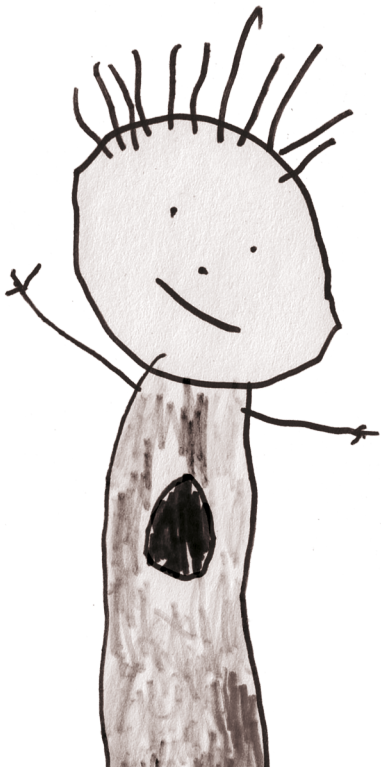
CHAPTER

8

THE IMPACT OF NUTRITIONAL STATUS ON HEALTH-RELATED QUALITY OF LIFE OF CHILDREN WITH CANCER

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Submitted



ABSTRACT

Purpose: Malnutrition in childhood cancer patients has been associated with lower health-related quality of life (HRQOL). However, this association has never actually been tested. Therefore, we aimed to assess the impact of nutritional status on HRQOL of children with cancer.

Patients and methods: In 104 children, aged 2-18 years and diagnosed with hematological, solid, or brain malignancies, nutritional status and HRQOL were assessed at diagnosis and at 3, 6, and 12 months using the child- and parent-report versions of the PedsQL 4.0 Generic scale and the PedsQL 3.0 Cancer Module. Scores on both scales range from 0-100.

Results: Undernourished children (BMI or fat free mass < -2SDS) reported significantly lower PedsQL scores compared with well-nourished children on the domains physical functioning (-13.3), social functioning (-7.0), cancer summary scale (-5.9), and nausea (-14.7). Overnourished children (BMI or fat mass > 2SDS) reported lower scores on emotional (-8.0) and cognitive functioning (-9.2) and on the cancer summary scale (-6.6); whereas parent-report scores were lower on social functioning (-7.5). Weight loss (>0.5 SDS) was associated with lower scores on physical functioning (-13.9 child-report and -10.7 parent-report), emotional (-7.4) and social functioning (-6.0) (child-report), pain (-11.6), and nausea (-7.8) (parent-report). Parents reported worse social functioning and more pain in children with weight gain (>0.5 SDS).

Conclusion: Undernutrition and weight loss were associated with worse physical and social functioning; whereas overnutrition and weight gain affected the emotional and social domain of HRQOL. Measures that improve nutritional status will contribute to enhanced health outcomes in children treated for cancer.

INTRODUCTION

A poor nutritional status during treatment for childhood cancer not only has substantial clinical implications, but also adversely affects a child's quality of life. Both undernutrition and overnutrition are common in children treated for cancer and can lead to more complications, higher relapse rates, and lower survival rates.¹⁻³ Metabolic alterations, reduced intake, and increased losses, due to vomiting and diarrhea, can result in weight loss and undernutrition.⁴ At the same time, weight gain and alterations in body composition have frequently been reported in this particular patient group.⁵⁻⁷

During the last two decades, improved survival rates have resulted in increased emphasis on children's personal needs. As a result, health-related quality of life (HRQOL) of children with cancer has become a critical issue in clinical practice. The use of intensive treatments combining chemotherapy, surgery, and radiation causes many side effects which negatively affect children's HRQOL.⁸ Generally, it is assumed that HRQOL in undernourished patients is lower compared with well-nourished patients⁹ and that improvement of nutritional status will contribute to a better HRQOL. However, this association between nutritional status and HRQOL in children treated for cancer has never been tested.

In adult cancer patients, undernutrition and weight loss have been linked with lower scores on all domains of HRQOL.¹⁰⁻¹² Furthermore, overnutrition in healthy children has been linked to lower HRQOL scores as well. Whether overnutrition has negative consequences for HRQOL in children treated for cancer is unknown.

The current study is the first to explore the association between nutritional status and HRQOL in children treated for cancer. HRQOL in children is preferably measured using both child self-report and parent proxy-report.^{13,14} Children and parents do not necessarily have similar views on the impact of the disease.¹⁵ Nevertheless, both reports provide valuable and complementary information towards a better understanding of the child's HRQOL. The objective of this study is to quantify the impact of undernutrition, overnutrition, weight loss and weight gain on HRQOL in a heterogeneous sample of childhood cancer patients during the first year after diagnosis.

METHODS

Participants

Participants were children between 2-<18 years of age who were diagnosed with cancer between September 2007 and December 2009 and who were willing to participate in the PeCanNut (Pediatric Cancer and Nutrition) study⁵ of the Pediatric Oncology Department of the University Medical Center Groningen (UMCG). Eligible patients were able to understand the Dutch language, received curative treatment, and were aged ≥ 5 years for child-report of HRQOL or were aged ≥ 2 years for parent proxy-report. A total of 128 patients met the inclusion criteria, of which 109 were aged ≥ 5 years. Reasons for attrition are presented in Figure 1. Ethical approval was obtained from the Medical Ethics Committee of the UMCG, and both parents and children aged ≥ 12 years gave their written consent.

Procedure

Measurements were taken at diagnosis, and at 3, 6, and 12 months after diagnosis. The follow-up measurements were taken between courses of chemotherapy to make participation more acceptable to patients.

Measures

Nutritional status

Weight, height and body mass index (BMI) were assessed and expressed as standard deviation scores (SDS) calculated from Dutch reference standards.^{16,17} Furthermore, fat free mass (FFM) and fat mass (FM) were based on bioelectrical impedance analyses (BIA) using a 50 kHz frequency BIA (BIA 101, Akern, Italy) and were expressed as SDS using Dutch reference values.¹⁸ Details regarding measurements have been published previously.⁵ Undernutrition was defined as BMI<-2SDS or FFM<-2SDS, and overnutrition as BMI>2SDS or FM>2SDS. Children with both FFM<-2SDS and FM>2SDS and children aged <4 years were solely classified based on BMI. Changes in weight following the previous measurement were expressed in changes in weight-for-age (WFA) SDS and as such controlled for normal growth during the study period. Relevant weight loss or weight gain was defined as >0.5 SDS WFA change. A 0.5 SDS increase or decrease corresponded to a weight change of up to 5%. In children with cancer, weight loss >5% was found to be associated with increased infection rates (E. Loeffen 2014). In adult patients, 5% weight loss is also used as criterion for critical weight loss.¹⁹

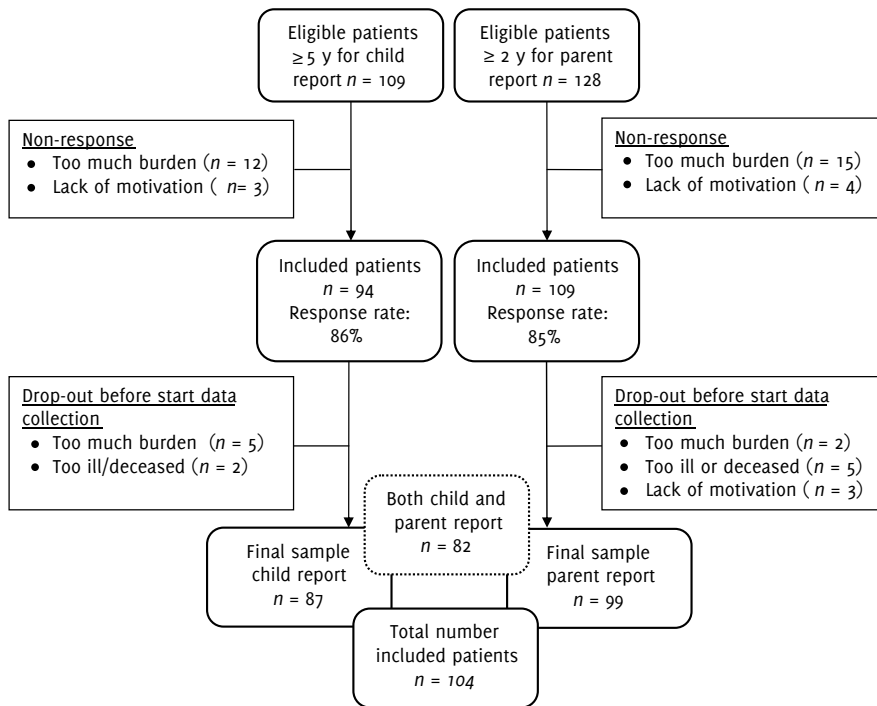


Figure 1. Flowchart patient inclusion for child and parent report

Health-related quality of life

The PedsQL measures are comprised of parallel child self-report formats (ages 5 and older) and parent proxy-report formats (ages 2 and older). The PedsQL 4.0 Generic Core Scale^{20,21} is a 23-item, multidimensional scale designed to measure generic HRQOL and includes 4 subscales: physical, emotional, social, and school functioning. The subscales can be summed into total scale scores, and psycho-social summary scores (composed of emotional, social, and school subscales).

The PedsQL Cancer Module²² is a 27-item scale developed to measure cancer specific HRQOL in children and includes 8 subscales: pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance, and communication. A total scale score and scores for the subscales pain and hurt, nausea, cognitive problems, and perceived physical appearance were calculated. These subscales were considered to be relevant in relation to nutritional status.

To improve interpretability of the scores, the items of the 5-point Likert scale were reversed and converted to a 0-100 scale following standard procedures²³ so that higher scores indicated better HRQOL. Both PedsQL instruments have high levels of reliability and validity.^{20-22,24}

Demographic and medical characteristics

The following patient characteristics were included in the analyses: age, gender, socioeconomic status (SES), type of malignancy, treatment severity, and treatment phase. Treatment severity was measured with the Intensity of Treatment Rating Scale (ITR-3).²⁵ Treatment phase was expressed as being on-active treatment or off-treatment. Education level of the father was included as a proxy for SES and stratified into three categories (low vocational education; intermediate vocational or general secondary education; higher professional or university education).

Data analysis and statistics

Prevalence rates of undernutrition, overnutrition and the number of patients with relevant weight loss or weight gain were calculated. The course of the PedsQL scales over time was estimated using unconditional growth models (Mixed models in SPSS). Paired t-tests were performed to compare child-report scores and parent-report scores.

In order to develop a powerful model and to prevent multiple testing by separate analyses at every measurement time, the association between undernutrition, overnutrition, weight changes and HRQOL was analyzed using multilevel analyses (Mixed models). We developed two series of predictive models of HRQOL as a function of time: one including categories undernourished, overnourished, and well-nourished as predictors, and one including weight loss, weight gain, and stable weight as predictors. Nutritional status was tested both for main effects and interaction effects with time. Time was expressed as time in months. The well-nourished and stable weight groups were used as reference categories. The demographic factors and medical characteristics were included as co-variables. These were first univariately tested for their association with either nutritional status or HRQOL by adding the variables to the unconditional growth model. Based on likelihood ratio tests, the co-variables were selected for inclusion in the multivariate multilevel analyses. In the analyses with weight change as a predictor, BMI SDS at diagnosis was included to control for the difference in impact of weight changes in lean or obese children. To compare the outcomes of the conditional growth models

of child self-report and parent proxy-report HRQOL, multilevel analyses of parent-report HRQOL were performed twice: once for all parent-report data (age children 2-18 years) and once for those cases with available child-report data (age children 5-18 years). All cases, including cases with missing data, were included for analyses. Analyses were performed using IBM SPSS Statistics 20. Statistical significance was accepted at the 5% level.

RESULTS

Characteristics of the cohort

In total, 104 patients (aged 2-18 years) diagnosed with hematological (43%), solid (33%), or brain malignancies (24%) participated in the study (Table 1). Of 87 patients, child-report data of the PedsQL were available, and of 99 patients parent-report data were available at any given measurement time (Figure 1). The majority of the patients received moderately intensive or very intensive treatment.

Descriptives nutritional status and health-related quality of life

Nutritional status

Percentage undernourished patients (BMI or FFM < -2SDS) decreased from 19% at diagnosis to 10% after 12 months; whereas for overnourished patients (BMI or FM > 2SDS) these figures were 9% to 18%, respectively. When using only BMI to define nutritional status, 8% to 1% was undernourished and 5% to 11% was overnourished at diagnosis and 12 months respectively. Twenty-eight percent of the patients experienced weight loss (>0.5 SDS WFA); whereas 37% gained more than 0.5 SDS WFA in the measurement period. On average, 15% (range 0%-36%) of the patients were classified as malnourished in both classifications; they were either undernourished and experienced >0.5 SDS weight loss or gain, or overnourished and experienced >0.5 SDS weight loss or gain. Details regarding the nutritional status of this cohort have been presented more extensively elsewhere.⁵

Health-related quality of life

HRQOL improved during the study period. PedsQL total child-report improved from 67.4 (SD 18.2) at diagnosis to 77.6 (SD 15.5) after 12 months (estimate slope .90 per month, 95% CI .59; 1.21, P < .001). PedsQL total

Chapter 8

Table 1. Patient characteristics (n=104)

Characteristic	
Age median (range)	9.0 (2.0-17.7)
	n (%)
Gender: female	56 (54)
Diagnosis:	
Hematological	45 (43)
Leukemia	33 (32)
ALL	28 (27)
AML	5 (5)
Lymphoma	12 (12)
Solid tumors	34 (33)
Neuroblastoma	7 (7)
Wilms tumors	5 (5)
Bone	8 (8)
Solid other	14 (14)
Brain tumors	25 (24)
Medullo- and ependymoblastoma	6 (6)
Astrocytoma/glioma	9 (9)
Craniopharyngioma	4 (4)
Other	6 (6)
Intensity of Treatment Rating (ITR)	
Least intensive	6 (6)
Moderate intensive	51 (49)
Very intensive	43 (41)
Most intensive	4 (4)
Education level father ^a	
Low vocational education	26 (25)
Intermediate vocational/general secondary education	45 (43)
Higher professional/university education	25 (24)

^a Education level of the father was used as a proxy for socioeconomic status. For 8 respondents data about education level were missing.

parent-report improved from 59.1 to 73.7 (estimate slope 1.12 per month, 95% CI .74; 1.51, $P < .001$). Scores on PedsQL Cancer Module improved from 75.0 (SD 15.5) to 82.1 (SD 12.0) (estimate slope .59 per month, 95% CI .33; .86, $P < .001$) and from 71.9 (SD 14.3) to 82.0 (SD 14.7) (estimate slope .74 per month 95% CI .48; 1.01, $P < .001$) for child- and parent-report respectively. Parent proxy-report scores were lower than child-report scores on total PedsQL at all measurement times ($t = 2.41$ to 4.08 , all P values < 0.05) and on the PedsQL Cancer Module at diagnosis and at 3 months ($t = 2.34$, $df = 74$, $P = 0.022$ and $t = 2.01$, $df = 67$, $P = 0.041$ respectively).

Co-variable testing

Univariate testing showed that type of malignancy and phase of treatment were related to nutritional status: children with brain malignancies had higher FM and lower FFM than children with hematological and solid malignancies, and children on-treatment had lower FFM than children off-treatment. Age, gender, type of malignancy, and phase of treatment were associated with HRQOL: older children, girls, children with brain malignancies, and children on-treatment reported lower HRQOL on one or more of the PedsQL summary scales or subscales. No relationship was found between SES or treatment intensity and HRQOL. Age, gender, type of malignancy, and phase of treatment were therefore included in the multilevel analyses to test whether differences in PedsQL scores were related to nutritional status or to one of the co-variables.

Association between nutritional status and HRQOL

Multilevel analyses showed no interaction between nutritional status and time; thus the trajectories of change in HRQOL over time were not significantly different for under-, over-, and well-nourished children (Figures 2a-2d, 3a-3d) and for children with weight loss, weight gain and stable weight. Therefore, only main effects are reported. The results of the analyses of all parent-report data (ages 2-18 y) and parent-report data of children 5-18 years were similar. Therefore, the results of the analyses of all parent-report data are presented.

Undernutrition

Undernourished patients reported significantly lower total PedsQL scores (-6.0 , $P = 0.003$) (child-report) than well-nourished patients (Table 2, figure 2a.). The differences were reflected in both physical and social functioning: undernourished patients scored 13.3 ($P = 0.006$) and 7.0 ($P = 0.014$) points

Table 2. Association between nutritional status and HRQL child-report (n=8) based on two separate multilevel analyses.^a The 1st and 2nd estimate represent the differences in PedsQL scores of under- or overnourished children compared with well-nourished children (reference group). The 3rd and 4th estimate represent the differences in PedsQL scores of children with weight loss or weight gain compared with children with stable weight (reference group).

	Reference group: well-nourished				Reference group: stable weight							
	Undernourished ^b		Overnourished ^c		Weight loss ^d		Weight gain ^d					
	Estimate	95%CI	P	Estimate	95%CI	P	Estimate	95%CI	P			
PedsTotal	-6.0	-11.6; -5	.003	-6.0	-12.3; .4	.065	-7.2	-12.4; -1.9	.008	-6	-5.2; 4.1	.812
Peds Physical	-13.3	-22.9; -3.8	.006	-7.9	-18.7; 2.9	.151	-13.9	-23.3; -4.6	.004	1.5	-6.7; 9.7	.724
Peds Psycho-social	-2.4	-7.1; 2.3	.319	-5.4	-10.8; -1	.046	-4.2	-8.6; .2	.062	-2.6	-6.5; 1.3	.186
Peds Emotional	3.3	-3.1; 9.9	.303	-8.0	-15.2; -8	.029	-7.4	-14.2; -.7	.032	-5.3	-11.2; .7	.083
Peds Social	-7.0	-12.6; -1.4	.014	-6.1	-12.4; .1	.054	-6.0	-11.1; -1.0	.020	-2.4	-6.8; 2.1	.296
Peds School	-2.9	-10.6; 4.9	.467	-4.0	-12.6; 4.5	.354	.27	-7.7; 8.3	.947	-1.4	-8.5; 5.7	.694
Peds Cancer	-5.9	-10.6; -1.3	.013	-6.6	-11.8; -1.4	.013	-9	-5.5; 3.7	.701	1.7	-2.3; 5.8	.397
Pain	-1.4	-11.4; 8.7	.788	-4.6	-15.5; 6.2	.401	-7.8	-19.0; 3.4	.170	4.0	-5.9; 13.9	.423
Nausea	-14.7	-22.7; -6.6	.000	-5.5	-14.3; 3.4	.225	1.4	-6.9; 9.7	.738	5.7	-1.6; 13.1	.126
Cognition	-4.5	-10.9; 1.9	.164	-9.2	-16.6; -1.9	.014	-4	-6.7; 6.0	.913	-5.3	-11.0; .3	.064
Appearance	-1	-8.0; 7.7	.972	-5.6	-14.4; 3.2	.209	1.9	-6.0; 9.8	.632	1.9	-5.1; 8.8	.596

^a Dependent variable PedsQL, independent variable nutritional status divided into 3 groups: undernourished, overnourished, and well-nourished; or weight loss, weight gain, stable weight. Reference category: well-nourished or stable weight. Included co-variables are: age, gender, type of malignancy, and phase of treatment.

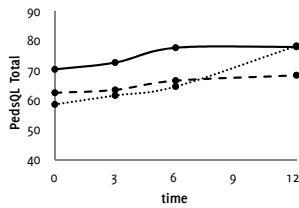
^b Based on BMI < -2SDS or FFM < -2 SDS.

^c Based on BMI > 2SDS or FM > 2 SDS.

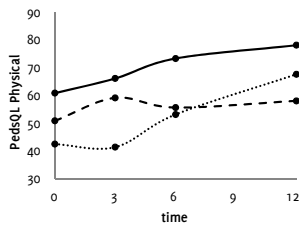
^d Weight loss or weight gain > 0.5 SDS.

Abbreviation: CI, confidence interval.

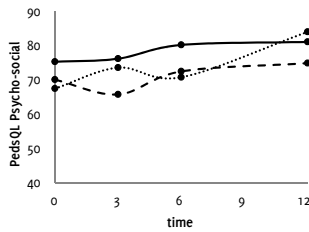
Figure 2.



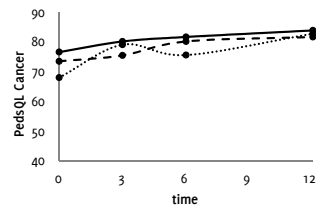
2a. PedsQL Total child-report



2b. PedsQL Physical child-report

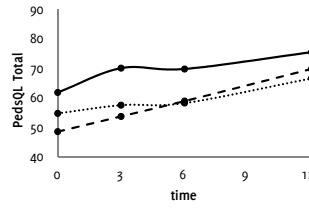


2c. PedsQL Psycho-social child-report

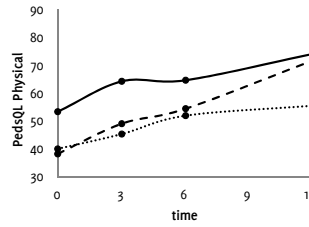


2d. PedsQL Cancer child-report

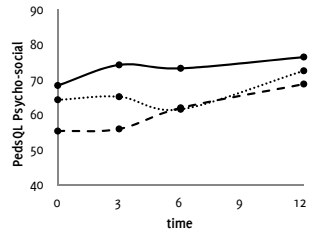
Figure 3.



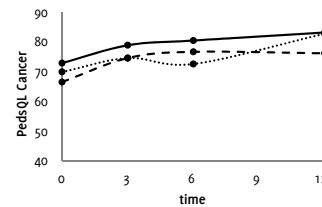
3a. PedsQL Total parent-report



3b. PedsQL Physical parent-report



3c. PedsQL Psycho-social parent-report



3d. PedsQL Cancer parent-report

— well-nourished
 undernourished
 --- overnourished

Figure 2 and 3 represent the trajectories of the PedsQL scores, based on child- or parent-report, for well-nourished, undernourished (BMI or FFM < -2SDS), and overnourished (BMI or FM > 2 SDS) children. The composition of the groups under-, over-, and well-nourished varied per measurement time: e.g. a patient could be in the undernourished group at diagnosis and in the well-nourished group at 3 months after diagnosis.

Table 3. Association between nutritional status and HRQL parent-report (n=99) based on two separate multilevel analyses.^a The 1st and 2nd estimate represent the differences in PedsQL scores of under- or overnourished children compared with well-nourished children (reference group). The 3rd and 4th estimate represent the differences in PedsQL scores of children with weight loss or weight gain compared with children with stable weight (reference group).

	Reference group: well-nourished				Reference group: stable weight				
	Undernourished ^b			Overnourished ^c	Weight loss ^d		Weight gain ^d		
	Estimate	95%CI	P	Estimate	95%CI	P	Estimate	95%CI	P
PedsTotal	-3.0	-9.6; 3.6	.372	-6.0	-13.7; 1.6	.122	-8.3	-15.0; -1.5	.016
Peds Physical	-8.2	-18.1; 1.7	.104	-4.9	-16.3; 6.6	.402	-10.7	-20.6; -8	.034
Peds Psycho-social	-8	-6.6; 5.0	.778	-7.5	-14.3; -8	.028	-5.2	-11.4; -.93	.096
Peds Emotional	.3	-7.0; 7.7	.927	-6.5	-15.2; 2.1	.135	-4.1	-11.4; 3.3	.275
Peds Social	-3.6	-9.7; 2.6	.253	-7.5	-14.7; -2	.043	-6.1	-12.3; -.1	.052
Peds School	1.9	-8.1; 12.0	.708	-8.2	-19.4; 3.0	.150	-10.2	-20.8; .5	.061
Peds Cancer	-0	-4.9; 4.8	.988	-4.2	-10.1; 1.6	.156	-3.1	-7.9; 1.7	.205
Pain	3.8	-5.6; 13.3	.426	-9.4	-20.3; 1.6	.093	-11.6	-21.4; -1.8	.021
Nausea	-6.4	-14.2; 1.4	.108	-4.1	-13.4; 5.1	.376	-7.8	-15.3; -.3	.041
Cognition	2.7	-4.7; 10.0	.477	-5.4	-14.3; 3.4	.227	.9	-6.6; 8.5	.811
Appearance	-4.6	-12.4; 3.1	.239	-8.5	-17.6; .5	.065	-2.5	-9.8; 4.7	.493
							-3.1	-9.8; 3.5	.352
							-6.6	-13.5; .3	.060
							-9.2	-18.4; -.0	.049
							-1.6	-6.0; 2.7	.463
							-3.7	-13.3; 5.9	.449
							-6.0	-11.7; -.3	.040
							-2.5	-9.3; 4.3	.470
							-6.1	-12.3; .1	.052
							-10.2	-20.8; .5	.061
							-3.1	-7.9; 1.7	.205
							-11.6	-21.4; -1.8	.021
							-7.8	-15.3; -.3	.041
							.9	-6.6; 8.5	.811
							-2.5	-9.8; 4.7	.493

lower respectively. Undernourished patients also reported lower scores on the PedsQL Cancer Module (-5.9, $P=0.013$) and the subscale nausea (-14.7, $P<0.001$). Parent report revealed no significant differences between under- and well-nourished patients on either one of the PedsQL scales (Table 3).

Overnutrition

Overnourished patients scored 5.4 points lower ($P=0.046$) on the psycho-social summary scale (child-report) than well-nourished patients (Table 2, figure 2c). This difference was reflected in both emotional functioning (-8.0, $P=0.029$) and social functioning (-6.1, $P=0.054$). Overnourished patients reported lower scores on the PedsQL Cancer Module (-6.6, $P=0.013$) and the subscale cognitive problems (-9.2, $P=0.014$). Parents of the overnourished patients scored lower on the psycho-social summary scale (-7.5, $P=0.028$) and on social functioning (-7.5, $P=0.043$) (Table 3). Overnourished patients also scored lower on physical functioning; however, the differences were not statistically significant.

Weight loss

Children with weight loss (>0.5 SDS) scored 7.2 points lower ($P=0.008$) on total PedsQL (child-report) compared with children with stable weight (Table 2). They scored lower on physical (-13.9, $P=0.004$), emotional (-7.4, $P=0.032$), and social functioning (-6.0, $P=0.020$) (Table 2). No differences were found for the PedsQL Cancer Module. Parent reports were lower for PedsQL total (-8.3, $P=0.016$) and for physical functioning (-10.7, $P=0.034$) (Table 3). Furthermore, parents reported more pain (-11.6, $P=0.021$) and nausea (-7.8, $P=0.041$) in children with weight loss.

Weight gain

Children with weight gain (>0.5 SDS) had similar PedsQL scores on all scales compared with children with stable weight (child-report). Parent-reports of children with weight gain were 6.0 points lower ($P=0.040$) on social functioning and 9.2 points lower ($P=0.049$) on pain.

DISCUSSION

This is the first study to explore the association between nutritional status and HRQOL in children treated for cancer. The results of the Pecannut study indicate that both undernourished children and overnourished children experienced worse HRQOL compared with well-nourished children. Significant weight loss and weight gain also contributed to worse HRQOL. To date, several studies have demonstrated worse HRQOL in undernourished adult cancer patients.^{11,12,26-28} However, to our best knowledge, the association between overnutrition and HRQOL has never been studied in cancer patients (adults or children).

Previous studies have shown that children treated for cancer have the lowest HRQOL when compared with healthy children or children with other diseases.^{20,29-31} The current study, however, demonstrates that under- and overnourished patients had the poorest HRQOL of all cancer patients. When examining the domains of HRQOL, impaired physical functioning was most prevalent in undernourished children and children with weight loss. It is well-known that undernutrition and weight loss are associated with loss of muscle mass and muscle weakness, resulting in fatigue.³² Hence, undernourished children lacked the energy and muscle strength to participate in physical activities. In addition, undernourished children reported more side effects of treatment: they had lower scores on the PedsQL Cancer Module, and experienced more pain and nausea. Pain and nausea have also been associated with fatigue,³³ which impairs children's ability to cope with side effects of treatment. Furthermore, tolerance for (toxicity of) chemotherapy may be less in undernourished patients,⁴ resulting in more side effects. Finally, undernourished children reported impaired social functioning. This finding can be explained by the pain, nausea, and fatigue these children experience, which impairs their ability to fully participate in physical and social activities with peers.

Compared with well-nourished children, overnourished children and children with weight gain reported worse functioning in the psycho-social domain, in particular in emotional and cognitive functioning; whereas parent-report scores were lower on social functioning. This implies that overnourished children "did not feel well": they were more vulnerable to feelings of fear, sadness, and anger; experienced more difficulties in the interaction with other children; and experienced more difficulties in performing cognitive

tasks than well-nourished children with cancer. A literature review³⁴ on HRQOL in healthy obese children and adolescents found that overweight had a negative impact on social and emotional functioning. Thus, the negative consequences of overweight in healthy children also apply to children with cancer. Contrary to obese healthy children, overnourished cancer patients did not experience worse physical functioning than well-nourished patients. It is likely that the impact of cancer and its intensive treatment on the children's physical functioning exceeded the impact of differences in nutritional status. Notably, overnourished children scored lower on cognitive functioning; whereas undernutrition is expected to be associated with lower performance on cognitive tasks.³⁵

An additional finding of this study was that children and parents reported differently on the impact of nutritional status on HRQOL. The most significant difference between child- and parent-report concerned the HRQOL of undernourished children: children reported significant impairments in several domains of HRQOL; whereas parent-report ratings failed to demonstrate differences between under- and well-nourished children. The fact that child- and parent-report had different outcomes does not reflect the lack of validity of either child- or parent-report, but rather reflects the different perspectives of children and parents on the child's HRQOL.³⁶ For example, children's perceptions are based on their subjective personal experiences with regard to symptoms such as fatigue, nausea, and pain. Children suffer from their undernourishment at first hand; whereas parents' view of their child's HRQOL is more indirect and relies on their external observations and on communication with the child.³⁷

Consistent with the literature,^{14,37,38} in the current study parent HRQOL ratings were lower than children's ratings. Parents are often more well-informed about treatment and prognosis, and they perceive cancer to have more negative consequences than children themselves. Moreover, their views may be influenced by the burden of care-giving, their own well-being, and other concerns.¹⁴ Nevertheless, the perspectives of both children and parents complement each other and increase our understanding of the association between nutritional status and the child's HRQOL.

Despite the fact that the current study concerned one of the largest prospective cohorts of children treated for cancer, the number of under- or overnourished patients at every single measurement time was relatively small. Therefore, to improve statistical power multilevel analyses were performed including all 4 measurement times.

This study demonstrated that during treatment HRQOL in undernourished patients and patients with weight loss is significantly lower than in well-nourished patients. However, overnourished patients and patients with weight gain were also more vulnerable to negative feelings and performed worse in several domains of HRQOL. These findings stress the importance of adequate nutritional care during treatment. Nutritional care as component of supportive care not only contributes to fewer complications and higher survival rates, but also contributes to better HRQOL outcomes in children treated for cancer. Finally, this study shows the added value of hearing both the children's and the parents' voices towards a better understanding of children's HRQOL.

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