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Normalized measures and patient characteristics to identify undernutrition in infants and young children treated for cancer

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SUMMARY

Background: Various measures and definitions for undernutrition are used in pediatrics. Younger children treated for cancer are at high risk, but lack well-defined risk-based screening and intervention.

Methods: A retrospective study collected weight longitudinally for patients less than three years-old over two years after initiating cancer treatment. We included those diagnosed 2007–2015 at a large pediatric cancer center. Exclusion criteria included treatment starting outside our system, secondary or relapsed malignancy, or incomplete information. A decrease ≥1 in weight-for-age or weight-for-height z-score signified clinically significant weight loss. Univariate and multivariate models assessed hazards for developing first episode of clinically significant weight loss.

Results: Of 372 patients, only 24.6% of patients lost 10% of weight, but 58.6% lost weight-for-age z-score ≥1 and 64.8% lost ≥1 weight-for-height z-score within two years of treatment initiation. Patients who lost weight were younger (median age 15 vs. 24 months, $p < 0.001$). Compared to patients diagnosed in the first year of life, those diagnosed 24–35 months were less

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Statement of authorship

DVR was the main researcher and primarily drafted the manuscript. ACM, KW-M, CMM, and BCP contributed to the study design and the writing of the study protocol. CEM assisted in study design and statistical plan with MW assisting in the statistical planning and data analysis. DVR performed the data collection with supervision by ACM and KW-M. Tables and figures were prepared by MW. Revision and approval of the final manuscript was performed by all authors.

Declaration of Competing Interest

The authors do not have a financial relationship with the organizations sponsoring this research that would create a real or perceived conflict of interest. The corresponding author has full control and ownership of the data presented here and can be produced for review by the journal if requested.

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likely to lose weight (HR 0.62, $p < 0.001$) and lost weight later (median time to weight loss 144 vs. 35 days). Higher treatment intensity increased weight loss risk (HR 2.30, $p < 0.001$) and decreased time to weight loss (35 vs. 154 days). No differences were found based on sex, diagnosis, enteral or parenteral nutrition, gastroenterology consults, or intensive care admissions.

Conclusions: Using normalized z-scores is more sensitive for identifying weight loss. Younger children are more likely to lose weight with higher intensity cancer therapy. Patient and treatment specific information should be used in risk stratifying weight loss screening and nutritional interventions.

Keywords

Cancer; Weight loss; Nutrition; Pediatric oncology; Infant; Anthropometric measures

1. Introduction

As outcomes in pediatric oncology continue to improve, focus has shifted to supportive care measures for children going through cancer treatment [1,2]. Treatment for certain pediatric cancers carries up to an 80% incidence of developing malnutrition, but most studies include patients from birth through young adulthood and a variety of diagnoses [3,4]. Children are at particularly high risk for poor nutrition during cancer treatment, which increases the risks of infection, mucositis, neutropenia, and worsens overall outcomes [5,6]. Poor nutrition has also been associated with impaired myelination, which is particularly important in neural development for infants and young children whose rapid growth, or lack thereof, can dramatically affect the metabolism of cancer drugs as well as future cognitive and functional development [7,8]. Unfortunately, there is little data on age or diagnosis-based risk for developing weight loss or malnutrition. In addition to lacking appropriate interventions to prevent and treat weight loss in children undergoing cancer treatment, consensus lacks on the appropriate measurement of weight loss in this age group.

Several validated screening tools for malnutrition in pediatric cancer patients exist, but variable methodology prevents generalization and consensus on ideal measures to be used specifically for undernutrition [9]. They also lack patient and disease specific risk factors for screening and intervention [10,11]. Pediatric malnutrition is defined broadly as an imbalance between caloric intake and expenditure, but undernutrition specifically refers to inadequate caloric intake compared to energy expended [12]. Additionally, the importance of disease and setting specific screening, including electronic based screening, has yet to be explored [13,14]. Biochemical assessments of nutrition including total protein, albumin or prealbumin, serum lipids, trace minerals, and vitamins has also been proposed but have not been studied in infants and young children undergoing cancer treatment [15,16]. The expected rapid growth in children, which is higher than adolescents or adults, is further impacted by cancer treatment, particularly emetogenic chemotherapy and radiation [17,18]. Since weight and height change quickly in children, standardized measurements are more important and representative of stunted growth than gross measurements.

The purpose of this study was to evaluate and compare different criteria for undernutrition including overall loss of body weight and change in standardized weight-for-age or weight-

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for-height z-scores. Our focus is specifically on infants and young children diagnosed less than three years of age because of the unique growth patterns in younger kids and the importance of proper nutrition early in life. Secondly, we aim to understand patient and treatment characteristics associated with higher risks of weight loss during cancer therapy. Identifying the characteristics associated with risk of weight loss will lay the groundwork for future research that examines the best timing for nutritional interventions in patients at-risk for weight loss.

2. Methods

2.1. Study design

This retrospective, observational cohort study included children less than three years old with newly diagnosed cancer between 2007 and 2015. Data were collected from the cancer registry and electronic medical record including primary diagnosis, age at diagnosis, treatment, and height and weight measurements monthly for the first year and quarterly through the second year following initiation of cancer treatment. Patients starting treatment outside a Children's Healthcare of Atlanta facility, diagnosed with a secondary or relapsed malignancy, or having inaccurate baseline measurements were excluded. Inaccurate measurements were determined by biologically implausible variables and verified with review (see below). The weight measured closest to the treatment initiation date (within 2 days of treatment initiation) was designated the baseline weight. Longer windows were considered, but rejected given the speed at which weight loss was seen to occur.

Normative data from the Centers for Disease Control (CDC) were used to standardize weight measurements to age and sex adjusted weight-for-age and weight-for-height z-scores using SAS® software (version 9.4). Biologically implausible values (BIV) using the CDC coding were individually reviewed and excluded if deemed inaccurate. Implausible values not resolved by manual chart review were set to missing in the final dataset. The BIV as defined by the CDC is used to identify extreme values that may be entered incorrectly, but not necessarily incorrect for an individual patient. Published rationale on criteria identifies z-scores as potentially biologically implausible if less than −5 or greater than 8 for WAZ or WHZ or height-for age less than −5 or greater than 4 [19].

Tumor type was classified as either "brain tumor," "hematologic malignancy," or "solid (non-brain) tumor," based on recorded diagnosis codes. Treatment intensity was assigned using Intensity of Treatment Rating (ITR-3), a validated and standardized rating scale which accounts for the overall effect of the total treatment received by a patient based on diagnosis and treatment modalities used [20]. Intensity ratings range from 1 (lowest intensity) to 4 (highest intensity). Treatment intensity was further grouped for analysis: low (rating of 1 or 2), medium (rating of 3), and high (rating of 4). Age group at diagnosis was also recorded and stratified into diagnosis at 0–11 months, 12–23 months, and 24–35 months.

Several definitions of clinically significant weight loss were examined (Table 2): a 10% decrease in weight, a 1 standard deviation (SD) decrease in weight-for-age z-score (WAZ), and a 1 SD decrease in weight-for-height z-score (WHZ). Based on the data, utilizing WAZ and WHZ to assess clinically significant weight loss was most appropriate due to a larger

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number of patients meeting those criteria. Additionally, using z-scores accounts for the expected growth in children. Setting 10% weight loss as the cut off for weight loss does not incorporate expected weight gain for patients growing and thus was not used in the definition of clinically significant weight loss.

2.2. Data preparation

Clinically significant weight loss was defined as a one standard deviation decrease from baseline in WAZ or one standard deviation decrease in WHZ based on the Consensus Statement of the American Academy of Nutrition and Dietetics [12]. A z-score loss of greater than or equal to 1 meets criteria for mild malnutrition. Although WHZ incorporates more information into the standardized scores than WAZ, we elected to evaluate both metrics as baseline height measurements are often missing in medical charts. Because children under the age of 1 year grow at a much faster rate than children over the age of 1 year for children under 1 year, height from a subsequent record was used if the record was within 14 days of the missing value [16,20]. For children over the age of 1 year, height from a subsequent record would be applied if within 30 days of the missing observation with the missing value.

Some patients had multiple weight values recorded in the same day, with one of the records being a BIV. For these patients, the BIV record was dropped in favor of the same-day biologically plausible values. Ten patients had a BIV for WAZ and did not have a second record on the same day. After manual chart review, the values for all ten were verified as correct and consistent with prior measurements in the medical record, thus retained in the analysis. Height measurements were recorded much less frequently than weight measurements. Patients with BIV for height readings did not have verifiable measurements and were set to missing height. When multiple values were recorded on a single day, they were averaged at the day level, except in cases of BIV.

For patients with a weight loss event, the time to first observed weight loss was used. Patients were censored at 2 years or last recorded visit was within two years of treatment initiation. If a patient was recorded as deceased, they were censored at the date of death. Clinical care information regarding nutritional treatment information was collected from the medical record. Variables extracted included months of enteral feeding, gastroenterology (GI) consults, intensive care unit (ICU) admissions, gastrostomy tube (GT) placement, and total parenteral nutrition (TPN) days.

2.3. Data analysis

Data were summarized as median (q1, q3) or N (%) in Table 1. Chi square or Fisher’s exact tests were used to test for differences between the weight loss and no weight loss groups for categorical variables. For continuous variables, Wilcoxon rank sums test was used to test for a relationship between the characteristic and weight loss group.

To examine factors associated with clinically significant weight loss, the outcome weight loss was treated as a time dependent variable and examined using survival analysis methods including both Kaplan Meier survival curves and Cox proportional hazard regression models. Variables examined in the Cox proportional hazard regression models included age,

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baseline weight for age, race, ethnicity, treatment intensity, diagnosis, months of enteral feeding, GI consult, number of ICU admissions, use of a G tube, and TPN days. In a univariate analysis, each possible risk factor was considered individually in a Cox proportional hazards model. Proportional hazards (PH) assumptions were examined using Schoenfeld weighted residuals. None of the variables violated the PH assumption. Variables significant at the 0.20 level in univariate analysis based on the Type III sums of squares tests were entered into a multivariable survival regression model, provided there were no issues with multicollinearity. Results from both the univariate and multivariable regressions are presented as hazard ratios with associated 95% confidence intervals. Because death is a competing event for significant weight loss, we re-examined the multivariable survival model using the Fine and Gray subdistribution hazard model in a sensitivity analysis. Additionally, a sensitivity test on our definition of weight loss, we ran the model using a different benchmark for weight loss (WAZ alone). Analysis was conducted using SAS v. 9.4 (SAS Institute, Cary, NC) and statistical significance was assessed at the 0.05 level, unless otherwise noted.

3. Results

Demographic information was examined with relation to those who developed clinically significant weight loss (Table 1). There was no difference in the proportion of patients who developed clinically significant weight loss based on sex, survival, ethnicity, or diagnosis category. Examination of the treatment intensity ratings demonstrated higher proportions of patients developing weight loss in the higher intensity groups ($p < 0.001$). Patients who experienced clinically significant weight loss during treatment were diagnosed younger (15 versus 24 months, $p < 0.001$). Although it approached statistical significance, there was no difference in the percentage of patients who died between the weight loss and no weight loss groups (24% vs. 15%, respectively; $p = 0.054$).

Table 2 summarizes results based on various definitions of weight loss used in clinical care. Of study patients, 24.6% had a 10% decrease in baseline weight during the study period. However, when assessing change in weight standardized for age and sex, 58.6% and 64.9% of patients met criteria for clinically significant weight loss (loss of greater than or equal to 1 SD) by WAZ and WHZ, respectively. Most patients who lost 10% of their body weight also met criteria for decrease in WAZ and WHZ (100% and 98.7%, respectively). Of the patients who met criteria for weight loss by WAZ or WHZ, less of those patients also met criteria for 10% weight loss (42.0% and 36.7%, respectively). Using the more sensitive measures for weight loss, a patient was deemed to have clinically significant weight loss if WAZ or WHZ decreased by greater than or equal to 1.

As a retrospective, observational study, we could not directly assess causality. However, certain characteristics associated with proper nutrition were identified before starting the study. These included baseline weight-for-age, months of enteral feeding, GI consults, ICU admissions, treatment intensity, ethnicity, GT placement, and days of TPN, in addition to the demographic factors described above. Univariate analysis was used to examine risk factors associated with weight loss, and variables with a p-value of less than 0.2 in the univariate analyses were included in the multivariable model (Table 3). In the full model, age, baseline

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weight-for-age, intensity, and ethnicity were significant, while enteral feeding, GI consultation, TPN, and ICU admissions were not. When compared to patients diagnosed in the first year of life, patients diagnosed at 24–35 months were less likely to develop clinically significant weight loss (HR 0.62, 95% CI 0.46–0.83, p = 0.002). Children diagnosed at 12–23 months old had a similar hazard ratio of 0.75 (95% CI 0.55–1.01) but did not reach statistical significance (p = 0.057). Patients with higher weight-for-age at treatment initiation also had higher odds of developing weight loss (HR 1.16, 95% CI 1.07–1.27, p < 0.001). Compared to patients who received low intensity treatment, there were higher odds of weight loss for patients in the medium intensity group (HR 1.67, 95% CI 1.25–2.23, p < 0.001) and high intensity group (HR 2.30, 95% CI 1.49–3.56, p < 0.001). Hispanic ethnicity was protective against weight loss (HR 0.68, 95% CI 0.47–0.98, p = 0.038). However, this effect was not significant in the sensitivity analysis using WAZ only as the weight loss definition (HR 0.88, 95% CI 0.60–1.30, p = 0.526).

Figure 1 illustrates the time to weight loss by age. Children diagnosed with cancer in the first year of life had a median time to first weight loss of 35 days (95% CI 24 – 52 days). Patients diagnosed 12–23 months old had a median time to first episode of weight loss of 82 days (95% CI 40 – 164 days). Children diagnosed 24–35 months old had the longest median time to first episode of significant weight loss at 144 days (95% CI 63 – 238 days). Treatment intensity also affected median time to first episode of weight loss with higher treatment intensity associated with shorter median time (Fig. 2).

The sensitivity analysis using the Fine and Gray subdistribution hazard model yielded similar results to the main model presented here.

4. Discussion

While multiple professional organizations and publications have called for improvement in screening for under nutrition, this study also emphasizes the importance of utilizing normalized measures of growth rather than raw evaluation of weight loss [5,21]. Additionally, the timing of weight loss in the study encourages that nutrition screening and intervention should occur within the first six months of initiating cancer treatment. Our data also reinforce children younger at diagnosis and treated with higher treatment intensity should receive even more focused attention to maintain optimal nutritional status.

Many metrics have been used for evaluating nutritional status including raw weight, growth velocities, weight-for-age, weight-for-height, trifold thickness, albumin, prealbumin, and several other validated nutrition screening tools [10,11,13–15,22,23]. In clinical care, body surface area is most often used for dosing chemotherapy in children, but absolute weight is used in infants and young children. Typically, a 10% weight loss is the trigger for modifying dosages and also serves as a concern for the patient's nutritional status [24]. Using only a decrease in body weight fails to account for the expected growth. Healthy children continually gain both height and weight through puberty. Additionally, in obese or overweight children, cancer cachexia can result in decreased muscle mass, worsening physical function, and increased treatment related toxicities, meaning weight loss to a normal weight during treatment may not necessarily be beneficial or safe [25]. Gross weight

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changes are particularly problematic in infants and young children in whom metabolism, height, and weight more rapidly change [16,23]. Our study suggests using standardized measures based on age and sex accounts for expected growth for children. We also demonstrate that WAZ and WHZ changes identify more patients than 10% change in body weight. This was used as our marker of clinically significant weight loss, but should be examined with other markers of nutrition in future studies. Estimates of malnutrition during pediatric cancer treatment vary widely with some estimates as low as 5% and other groups as high as 90% [4,26,27]. While only 24% of children in our study lost 10% of their weight after initial diagnosis, over 70% met criteria for clinically significant weight loss: either a weight-for-age or weight-for-height z-score decrease greater than or equal to one. Utilizing a change in z-score also incorporates the patients' individual size at treatment initiation, which is important in maintaining healthy weight through therapy. As many children receive steroids, radiation, or surgery during cancer treatment, providers should also consider body composition and metabolic changes that are occurring separately from body weight changes alone. Further research in body composition, including cancer cachexia and sarcopenia, in pediatric cancer patients is needed as well as standardized assessments in this population [28,37].

Examination of risk factors for weight loss demonstrated important patient and treatment characteristics. Univariate analysis found statistically significant differences in the hazards for developing clinically significant weight loss based on age at diagnosis, baseline weight-for-age, enteral feeding, gastroenterology consultation, ICU admissions, and treatment intensity ratings. When each was incorporated in the multivariate model, only age at diagnosis, baseline weight-for-age, and intensity rating are statistically significant. Interestingly, gastroenterology consults, parenteral nutrition, and enteral supplementation were not seen as protective against weight loss. As an observational study, causality and temporality are difficult to assess. In this patient population, we may not have seen lower odds of weight loss among those receiving supplemental nutrition for various reasons. Patients who are malnourished are more likely to receive parenteral and enteral supplementation. Similarly, patients who are not meeting their caloric intake goals may be more likely to be placed on nutrition supplementation prior to dropping more than one standard deviation in their z-score for weight-for-age or weight-for-height.

While treatment intensity has been demonstrated to affect weight loss, there are only a few studies examining the different toxicities experienced by patients based on age or diagnosis [4,21,27]. The lack of multivariate statistical significance suggests gastroenterology consultation, enteral feeding supplement, and ICU admissions are not independent risk factors for weight loss, but rather more likely accounted for by other factors in the multivariate model. Because intensity rating incorporates treatment related toxicity, it can act as a surrogate for the need for nutrition supplementation and subspecialty consultation. The fact that Hispanic ethnicity is only associated with a protective effect when WHZ is included in the definition of weight loss underscores the importance of establishing a standard definition of weight loss. The interrelationship of demographic characteristics, treatment effects, and nutritional interventions emphasizes the need for proactive study of weight loss screening and interventions for infants and young children treated for cancer.

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Several patient and treatment characteristics associated with higher odds of weight loss identify important aspects for risk stratification of patients based on nutritional risks. Age at diagnosis is a particularly interesting risk factor for weight loss, especially given age related differences in toxicities experienced during rhabdomyosarcoma or lymphoma treatment [29,30]. Our findings showed patients diagnosed in their first year of life had twice the odds of developing significant weight loss as those diagnosed 24–35 months of age with a median time of 35 days to the first episode of significant weight loss. The patients diagnosed 24–35 months of age had a lower incidence of weight loss and had a much longer median time to first event of weight loss. This finding supports previous research that the highest time period to develop significant weight loss is within the first several months of treatment [3,4]. However, it also highlights the need for more patient specific nutrition screening guidelines and intervention and has not been used in previous decision tools [10,11]. The data also demonstrates a 16% increase in odds of experiencing weight loss per 1 unit increase in weight for age suggesting that the larger patients are more likely to lose weight. While these patients have higher odds of developing weight loss, they may not necessarily experience more morbidity or mortality as the patients who start treatment with less than ideal nutritional status. More research is needed to better understand the degree and timing of weight loss.

Coupling age and nutritional status at diagnosis with treatment intensity may also allow providers to identify the patients at highest risk for losing weight and intervene earlier. While screening and treatment algorithms have been developed, data on successfully utilizing these tools in very young patients is scant [10,13,15]. Both patients with medium and high treatment intensity had about twice the odds of developing weight loss in the two years after treatment initiation. However, the timing until first episode of significant weight loss differed between the groups - higher intensity treatment having shorter median time to weight loss. The effect of nutritional status at treatment initiation further emphasizes the importance of patient-based risk stratification, screening, and intervention for under nutrition. Research has demonstrated outcomes improve with registered dietician involvement, as well as decreased hospital lengths of stay [9,31,32]. Applying these principles to children undergoing cancer therapy, especially the youngest patients, will allow more effective utilization of enteral and parenteral nutrition supplementation and risk directed resource utilization.

Although there are several limitations to this study, it identifies potential areas for future research and improved clinical care. First, as a retrospective and observational study, causality cannot be assigned. While associations with weight loss can be made, you cannot disconnect the intensity of treatment from the diagnosis itself. Additionally, height and weight are the only anthropometric measurements gathered as routine clinical care. The European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society for Parenteral and Enteral Nutrition (ASPEN) both recommend more comprehensive measurements including mid-upper arm circumference [33,34]. Height and weight alone fail to account for body composition, sarcopenia, and other nutritional changes due to steroids or radiation that should be considered in future prospective study. Second, our patient population is left truncated, meaning no patients can be identified before a diagnosis of a malignancy, so there may an effect of the tumor itself on the baseline characteristics or the

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response to the therapy. Finally, our patients are only observed for two years following treatment initiation. While over 70% of the patients were alive at the time of the study, there is no measure of long-term morbidities. Neural myelination is key early in life and the impact undernutrition has on cognitive, motor, and developmental outcomes cannot be assessed retrospectively [8]. While prior studies have linked poor nutrition during treatment to increased toxicities including bone health and neuropathy, this information was not available in our retrospective analysis. Our study does identify patients at risk for developing weight loss following treatment initiation, but the analysis did not distinguish duration of treatment within the two-year window of this study. Understanding that weight loss during therapy may be more likely, we have yet to elucidate the highest risk time periods for weight loss as well as potential problems for malnutrition and failure to thrive following treatment. As such, for this exploratory analysis, the two groups were not separated.

This information can be used to prospectively study and identify patients earlier in developing undernutrition while also mitigating the degree of weight loss and some associated short and long-term morbidities. These data ultimately reinforce the importance to risk-based stratification for patients. Proactively identifying the patients at highest risk for weight loss will allow for targeted and efficient interventions, especially in resource limited settings. Knowing that weight loss and nutrition supplementation can increase parental anxiety as well as hospital length of stay, better understanding is needed from a patient and societal perspective [32,35,36]. Ultimately, creating risk-based interventions can improve patient outcomes and family experiences.

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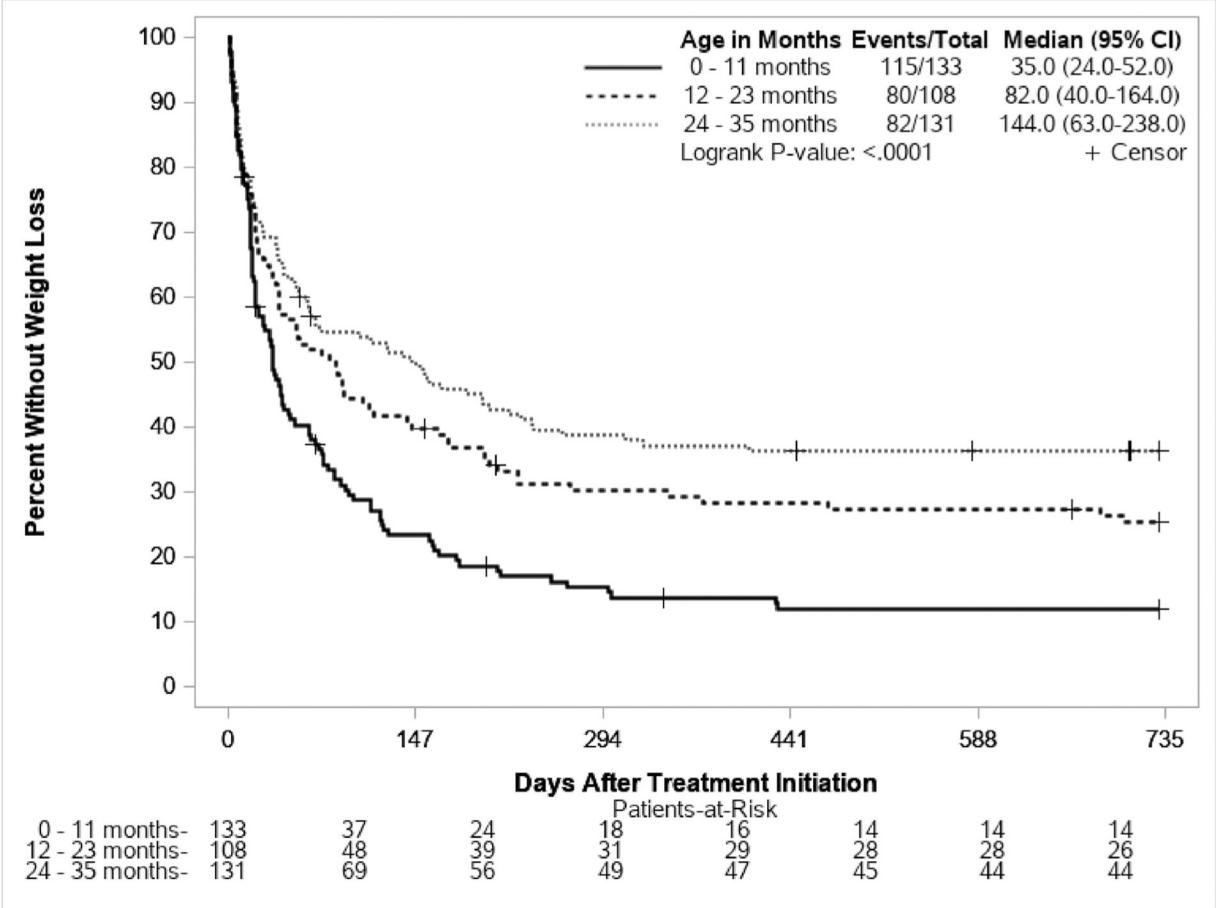

Fig. 1.
Weight-loss-free survival based on age at diagnosis.

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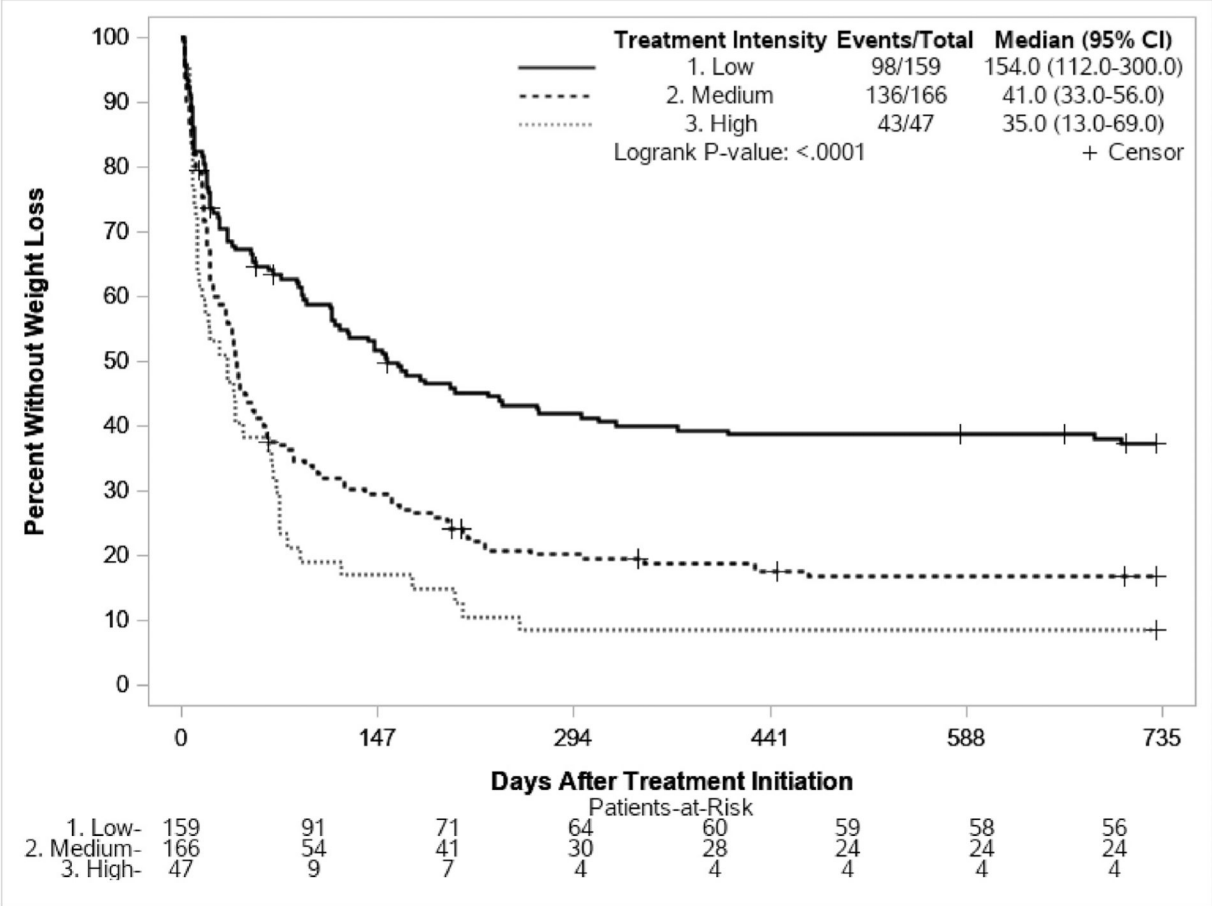

Fig. 2.
Weight-loss-free survival based on treatment intensity.

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Table 1:

Demographic patient features including weight loss status.

Variable	Level	Overall N = 372	No Weight Loss N = 95	Weight Loss N = 277	P-Value
Age in months *Median (Q1, Q3)*		17 (8, 26)	24 (14, 30)	15 (7, 25)	<**.001**
Sex	Female	184 (49.46%)	51 (53.68%)	133 (48.01%)	0.340
	Male	188 (50.54%)	44 (46.32%)	144 (51.99%)	
Race	Black	126 (34.05%)	27 (28.72%)	99 (35.87%)	0.362
	Other	23 (6.22%)	5 (5.32%)	18 (6.52%)	
	White	221 (59.73%)	62 (65.96%)	159 (57.61%)	
	Unknown	2 (0.54%)			
Ethnicity	Hispanic	54 (14.63%)	19 (20.21%)	35 (12.73%)	0.076
	Non-Hispanic	315 (85.37%)	75 (79.79%)	240 (87.27%)	
	Unknown	3 (0.81%)			
Diagnosis	Brain tumor	50 (13.44%)	14 (14.74%)	36 (13%)	0.881
	Hematologic malignancy	143 (38.44%)	37 (38.95%)	106 (38.27%)	
	Solid Tumor (non-brain)	179 (48.12%)	44 (46.32%)	135 (48.74%)	
Intensity Rating	1	17 (4.57%)	6 (6.32%)	11 (3.97%)	<**.0001**
	2	142 (38.17%)	55 (57.89%)	87 (31.41%)	
	3	166 (44.62%)	30 (31.58%)	136 (49.1%)	
	4	47 (12.63%)	4 (4.21%)	43 (15.52%)	
Vital Status	Alive	291 (78.23%)	81 (85.26%)	210 (75.81%)	0.054
	Dead	81 (21.77%)	14 (14.74%)	67 (24.19%)	

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Table 2:

Comparing definitions of weight loss.

Measure	Overall Percent Meeting Definition	Percent Meeting Additional Definitions		
		1 point drop in weight-for-height z-score (WHZ)	1 point drop in weight-for-age z-score (WAZ)	10% decrease in weight
10% decrease in weight	24.60%	98.70%	100.00%	N/A
1 point drop in weight-for-age z-score (WAZ)	58.56%	83.43%	N/A	42.01%
1 point drop in weight-for-height z-score (WHZ)	64.89%	N/A	72.95%	36.71%

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Table 3:

Risk factor analysis with hazard ratio for developing clinically significant weight loss during treatment.

Variable	Comparison	Hazard Ratio for Univariate Analysis (95% CI)	P-Value	Hazard Ratio for Full Model (95% CI)	P-Value
Age	0–11 months	Ref			
	12–23 months	0.67 (0.50, 0.89)	0.006	0.75 (0.55–1.01)	0.057
	24–35 months	0.52 (0.39, 0.69)	<0.001	0.62 (0.46–0.83)	0.002
Sex	Male	Ref		Omitted	
	Female	0.91 (0.72, 1.15)	0.415		
Baseline Weight for Age	Unit = 1	1.15 (1.05, 1.26)	0.002	1.16 (1.07–1.27)	<0.001
Months of Enteral Feeding	Unit = 1	1.07 (1.03, 1.11)	<0.001	1.00 (0.94–1.06)	0.999
GI Consults - At Least One	Yes	Ref			
	No	0.72 (0.55, 0.93)	0.011	0.88 (0.65–1.20)	0.431
Number of ICU Admits	Unit = 1	1.16 (1.05, 1.28)	0.005	1.03 (0.90–1.18)	0.641
Intensity Rating	1 & 2 (Low)	Ref			
	3 (Medium)	1.81 (1.39, 2.35)	<0.001	1.67 (1.25–2.23)	<0.001
	4 (High)	2.45 (1.70, 3.52)	<0.001	2.30 (1.49–3.56)	<0.001
Race	White	Ref			
	Black	1.19 (0.93, 1.53)	0.176	Omitted	
	Other	1.14 (0.70, 1.85)	0.606	Omitted	
Diagnosis	Solid tumor (non-brain)	Ref			
	Brain tumor	0.89 (0.62, 1.29)	0.548	Omitted	
	Hematologic malignancy	0.97 (0.75, 1.25)	0.804	Omitted	
Ethnicity	Non-Hispanic	Ref			
	Hispanic	0.74 (0.52, 1.05)	0.09	0.68 (0.47–0.98)	0.038
GTube	Yes	Ref			
	No	0.92 (0.61, 1.37)	0.674	Omitted	
TPN Days	Unit = 1	1.00 (1.00, 1.01)	0.039	1.00(0.99–1.01)	0.981