This author's PDF version corresponds to the article as it appeared upon acceptance. Fully formatted PDF versions will be made available soon.

Effect of nutritional status on outcomes in children receiving umbilical cord blood stem cell transplantation

doi: 10.6133/apjcn.202211/PP.0010
Published online: November 2022

Running title: Nutritional effects on outcomes in pediatric UCBT

Zhongying Lu BS[1†], Yongzhen Li MS[1,2†], Peng Shi MS[3,] Xiaoyan Gong BS[1], Yiyao Zhou BS[1], Xiaowen Qian PhD, MD,[4] Xiaowen Zhai PhD, MD[4], Tian Qian PhD MD[1]

[1]Clinical nutrition Department, Children's Hospital of Fudan University, Shanghai, China
[2]Clinical nutrition Department, New Hong Qiao Compus for Children's Hospital of Fudan University, Shanghai, China
[3]Pediatric Clinical Research Unit, Department of Research Management, Children's Hospital of Fudan University, Shanghai, China
[4]Hematology Department, Children's Hospital of Fudan University, Shanghai, China
[†]Both authors contributed equally to this manuscript

Authors' email addresses and contributions:
Zhongying Lu, Lzy20060502@163.com,
Yongzhen Li, liyz18@fudan.edu.cn,
Peng Shi, pengshi@fudan.edu.cn,
Xiaoyan Gong, xygongfudan@163.com,
Yiyao Zhou, kerry_zyy@yahoo.com,
Xiaowen Qian, qxw08@hotmail.com,
Xiaowen Zhai, zhaixiaowendy@163.com,
Tian Qian, drqiantian@fudan.edu.cn

Mrs. Zhongying Lu and Mrs. Yongzhen Li are the co-first authors, have contributed equally to this work, and are in agreement to be accountable for all aspects of the work. Mrs. Zhongying Lu contributed to the design of the study and the acquisition of the data and manuscript drafting. Mrs. Yongzhen Li, was involved in analysis and interpretation of data, paper drafting, designing and writing, the critical revision of the manuscript and approval of the final version for submission.
Dr. Tian Qian and Dr.Xiaowen Zhai are the co-corresponding authors and contributed to the conception and design of the study, revision of the manuscript, final approval of the version to be published and are in agreement to be accountable for all aspects of the work.
Mr. Peng Shi, Mrs. Xiaoyan Gong and Mrs. Yiyao Zhou contributed to the acquisition of the data, statistics methods help and are in agreement to be accountable for all aspects of the work.
Dr. Xiaowen Qian was involved in design of the study, revision of the manuscript, final approval of the version to be published and is in agreement to be accountable for all aspects of the work

Corresponding Author: Dr Tian Qian, Clinical nutrition Department, Children's Hospital of Fudan University, Shanghai, China, 201102. Email: drqiantian@fudan.edu.cn. Dr Xiaowen Zhai, Hematology Department, Children's Hospital of Fudan University, Shanghai, China, 201102. Tel: . Email: zhaixiaowendy@163.com

Not Proof Read

ABSTRACT

Background and Objectives: The impacts of nutritional status on clinical outcomes in children receiving umbilical cord blood stem cell transplantation (UCBT) are not fully described. We evaluated the risk for malnutrition before transplantation admission and influence of weight loss during hospitalization on short-term clinical outcomes in children with UCBT. **Methods and Study Design:** We conducted a retrospective study of pediatric patients up to age 18 years who received UCBT and were treated at the Children's Hospital of Fudan University between January 2019 and December 2020. **Results:** The mean age of the 91 patients was 1.3 years, with 78 (85.7%) men and 13 (14.3%) women (p<0.001). UCBT was performed mostly for primary immunodeficiency disease (PID) (83, 91.2%). The weight loss differences among children with different primary diseases were statistically significant (p=0.003). Children with a large amount of weight loss during hospitalization (n = 24) had higher risks of skin graft-versus-host disease (GVHD) (multivariate OR=5.01, 95% CI: 1.35-18.65), intestinal GVHD (multivariate OR=7.27, 95% CI: 1.74-30.45), a longer median hospital stay (p=0.004), higher antibiotic costs (p = 0.008) and higher total hospitalization costs (p=0.004). Malnutrition on admission was significantly positively correlated with longer parenteral nutrition (PN) time (p=0.008). Early nutritional intervention effects on clinical outcomes need further assessment. **Conclusions:** Recipient child underweight children and excessive weight loss during transplantation increases the length and cost of hospital stay, and is associated with a high incidence of GVHD, which affects the prognosis of transplantation and medical resources consumption.

Key Words: nutritional status, umbilical cord blood stem cell transplantation, malnutrition, weight-loss, China

INTRODUCTION

Umbilical cord blood haematopoietic stem cell transplantation (UCBT) has gradually become an important alternative to haematopoietic stem cell transplantation (HSCT) due to its wide availability, low incidence of post-transplantation complications, relatively low incidence of graft-versus-host disease (GVHD) and comparable survival rate with other types of HSCT.[1-3] UCBT can enable treatment of more than 80 diseases, such as haematological malignancies, genetic metabolic diseases and immunodeficiency diseases (IDs),[3,4] and has been widely used in recent years, especially in children. However, UCBT may lead to an increased risk of late

Not Proof Read

viral infections, which can be fatal, due to delays in immune reconstitution.[5] Therefore, it is very important to explore key influencing features which might influence UCBT outcomes.

Nutritional status before transplantation affects prognosis after HSCT.[6] Malnutrition is associated with increased mortality rates and medical costs, poor quality of life and prolonged hospitalization.[7,8] The side effects of stem cell transplantation (SCT), including vomiting, anorexia, diarrhoea and mucositis, can directly impair oral intake in the early post-transplantation period. Acute gastrointestinal GVHD, infections and medications, such as opioids, have also been correlated with decreased oral feeding.[9] These changes result in weight loss and the rapid deterioration of nutritional status, which is associated with adverse clinical outcomes. There is growing interest in supportive care, especially nutritional support for HSCT recipients, because nutritional support protocols may decrease the hospital length of stay, risk of mucosal barrier injury and weight loss.[10]

Controversies still remain as to whether weight loss and deterioration of nutritional status are associated with negative clinical outcomes in HSCT patients.[6,8,11-13] Although UCBT has progressed rapidly in recent years, there are few recent studies on nutrition-related transplantation outcomes. Therefore, the purpose of this study was to assess whether children's malnutrition risk at admission and weight loss during hospitalization for UCBT was associated with important clinical outcomes and to provide basic data to guide precision nutritional interventions in UCBT patients.

MATERIALS AND METHODS

Study design and participants

A single-centre, retrospective, descriptive study was conducted in paediatric patients receiving UCBT at the Department of Hematology and Bone Marrow Transplant Unit of the Children's Hospital of Fudan University between January 1, 2019, and December 31, 2020. The subjects were children of both sexes aged 0–18 years. Demographic and clinical information included age, sex, height, weight, primary disease diagnosis, time to platelet and neutrophil engraftment, enteral nutrition (EN) and parenteral nutrition (PN) implementation. Laboratory parameters were retrieved from electronic medical records (EMRs). Clinical outcomes of interest were GVHD, pneumonia, sepsis, intensive care unit (ICU) transfers, one-year mortality, time to granulocyte and platelet engraftment, length of hospitalization, total hospitalization, antibiotic and other costs. Figure 1 shows the study design in detail. This study was approved by the Human Investigation Committee of Children's Hospital of Fudan University (2021-4861).

Not Proof Read

A total of 276 paediatric patients who received SCT were initially enrolled. Patients with incomplete information in their EMRs, including missing height or weight records (149), and those who did not receive UCBT (36) were excluded. The final sample included 91 patients.

Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). BMI-Z values were calculated using an online BMI-Z value calculator that has been validated by the World Health Organization (WHO). Patients were classified into two categories depending on their BMI-Z values: the control group (Z>-1) and the malnutrition group (Z≤-1). Weight measurements were collected weekly during hospitalization. Weight loss was obtained by subtracting the weight at discharge from the weight at admission. Weight loss ≥7% during hospitalization was defined as the high weight loss group (group H), and weight loss <7% was defined as the low weight loss group (group L).[14,15]

Statistical analysis

Data analyses were performed with SPSS 25.0 (IBM SPSS Statistics for Windows, Version 25.0. IBM). Continuous variables are presented as the median (P25, P75) and mean ± standard deviation (SD), and categorical and nominal variables are presented as frequencies (percentages). Fisher's exact test and the chi-square test were used to analyse differences in categorical variables. The two-sample t test and Mann–Whitney U test were used to describe variable characteristics and identify the relationship between continuous variables in the different groups. Significance was set at $p<0.05$. Risk was calculated as the odds ratio (OR), and binary logistic regression was used for the multivariate analysis. The regression models were adjusted for age, sex, diagnosis, low calcium at admission, and nutritional status at admission, which were evaluated for multicollinearity at the same time.

RESULTS

Patient demographics and clinical characteristics

Patient characteristics in different weight loss groups are reported in Table 1. The sample included 78 (85.7%) boys and 13 (14.3%) girls, with a median age of 1.3 years (0.8, 3.6 years). A high malnutrition risk (BMI-Z value ≤-2) was identified in 20 patients (22%). The most common diagnoses were primary immunodeficiency disease (PID) (83, 91.2%), including 32 (35.2%) cases of inflammatory bowel disease (IBD), 22 (24.2%) cases of severe combined immunodeficiency (SCID), 1 (1.1%) case of Wiskott-Alarich syndrome (WAS), 18 (19.8%) cases of chronic granulomatous disease (CGD) and 10 (11.0%) cases of other

Not Proof Read

immune deficiency diseases. Other diagnoses included mucopolysaccharidosis (2, 2.2%) and adrenoleukodystrophy (6, 6.6%).

According to weight loss during hospitalization, group L (n=67) and group H (n=24) accounted for 73.6% and 26.4% of the total, respectively. The age of the children in group H (3.6 years, 1.9-6.9 years) was older than that in group L (1.2 years, 0.7-2.5 years) (p<0.001). There was no significant difference in the sex distribution between the two groups. A larger amount of weight loss was associated with a lower BMI-Z value at admission (p=0.025). There was a significant difference in weight loss of children with different primary diseases (p=0.003), and there was a moderate association between disease type and weight loss (Cramer's V=0.392).

There were 62 patients (68.1%) with low serum prealbumin, 11 (12.1%) with hypoalbuminemia and 8 (8.8%) with anaemia at admission, with no differences between the two groups. There was no significant difference in the interval from disease diagnosis to transplantation between the two groups (p=0.167), but the longer the interval from the onset of symptoms to transplantation, the greater the weight loss (p=0.031). Forty-one (45.1%) children received EN support, 57 (62.6%) received PN support during hospitalization, and there was no difference in EN (p=0.565) or PN (p=0.987) implementation among the different weight loss groups.

Clinical outcomes associated with weight loss

Weight loss during hospitalization was associated with poor clinical outcomes, as shown in Table 2. Thirty-two (47.8%), nine (13.4%) and three (4.5%) children receiving UCBT experienced skin, intestinal and liver GVHD, respectively. Patients with a large amount of weight loss had a higher risk of skin GVHD than those with a small amount of weight loss (univariate OR=3.28, 95% CI: 1.16-9.29, p=0.021), and the incidence of intestinal GVHD was also higher (univariate OR=3.87, 95% CI: 1.31-11.44, p=0.017). There was no significant difference in the incidence of liver GVHD between the two groups. After adjustment for variables in the logistical analysis, the risk of skin GVHD was higher in group H than in group L (multivariate OR=5.01, 95% CI: 1.35-18.65, p=0.016), the risk of intestinal GVHD was higher in group H (multivariate OR=7.27, 95% CI: 1.74-30.45, p=0.007). but the incidence of liver GVHD was not significantly different from that in group L.

There were no significant associations between weight loss amount and the incidence of pneumonia and sepsis, the time of granulocyte implantation, the time to platelet and neutrophil engraftment, PN duration, ICU transfers, and 1-year mortality after transplantation

Not Proof Read

in the different weight loss groups. The median length of hospitalization was 64.5 [interquartile range (IQR), 46.0-88.5] days, and patients with higher weight loss had a longer median length of hospitalization (94.0 IQR [65.8~117] vs 64.5 IQR [46~88.5]; p=0.004). Total hospitalization cost (0.370 [IQR, 0.260-0.502] million yuan vs. 0.263 [IQR, 0.200-0.320] million yuan, p=0.004) and antibiotic costs (84 [IQR, 64-137] thousand yuan vs. 63 [IQR, 54-84] thousand yuan, p=0.008) were higher in group H than in group L.

Effects of malnutrition at admission on clinical outcomes

According to the BMI-Z value of weight on admission, the children were divided into the control group (Z>-1, n=59) and the malnutrition group (Z≤-1, n=32). Malnutrition status on admission was associated with poor clinical outcomes (Table 3). For patients in the malnutrition group, the median length of PN duration was 14 (IQR, 8-40) days, which was longer than 3 (IQR, 0-18) days in the control group (p=0.008). The time to platelet and neutrophil engraftment, length of hospitalization, total hospitalization cost and antibiotic costs were not significantly correlated with nutritional status at admission. The multivariate analysis showed that malnutrition at admission was more likely to increase the risk of intestinal GVHD (OR=3.20, 95% CI: 0.90-11.80, p=0.08), but not significantly associated with liver or skin GVHD, pneumonia, sepsis, ICU transfers, or 1-year mortality.

DISCUSSION

The nutritional status of HSCT patients may affect the length of hospitalization, occurrence and severity of GVHD, mortality and other prognosis.[16-18] Our study found that children receiving UCBT with a large amount of weight loss had increased risks for skin, intestinal and liver GVHD development during hospitalization, prolonged hospitalization, and higher total hospitalization and antibiotic costs. Malnutrition at admission can prolong the time of PN. This suggests that UCBT patients may benefit from improved nutrition before or during hospitalization to prevent adverse clinical outcomes.

This study found that weight loss was associated with age, and group H included more older children than group L. This may be due to older children having a heavier weight, higher medication doses and a greater likelihood of psychological factors, such as abnormal eating behaviours, during transplantation, which can have a strong influence. The type of primary disease and the time from the onset of symptoms to transplantation also affect weight, and the later transplantation is performed, the more serious weight loss becomes.

Not Proof Read

Our finding that a large amount of weight loss was significantly associated with increased odds of prolonged length of hospitalization is consistent with Lazarow et al.'s findings.[15] Patients with a large amount of transplantation-associated weight loss experienced longer hospital stays (p<0.001) and more intensive care unit transfers than those with a smaller amount of weight loss (p=0.001). However, we did not demonstrate an obvious association between poor nutritional status at admission and length of hospitalization, which is different from previous studies on the nutritional status of children receiving HSCT.[7,19]

GVHD is the most common complication of UCBT. Acute GVHD mainly affects the skin, gastrointestinal tract and liver and usually occurs 2 to 42 weeks after transplantation. It manifests as widespread maculopapular rash, persistent anorexia, diarrhoea, jaundice and liver dysfunction.[20] Acute GVHD is a major fatal complication in the first few months after allogeneic HSCT, while chronic GVHD affects mortality and quality of life of patients.[21] The multivariate analysis in this study found that high weight loss during hospitalization was associated with an increased risk of skin and liver GVHD in children receiving UCBT. This is consistent with Eva et al.'s findings that low BMI or weight loss increased the risk of severe GVHD three- to-four fold in the following 30 days.[22] Therefore, it is necessary to provide nutritional treatment and monitor weight changes during the treatment process, and a nutritional support plan should be established by a multidisciplinary nutritional support team (NST). The determination of optimal nutrient intake can minimize the incidence of adverse outcomes in UCBT patients.

Infection and gastrointestinal complications (vomiting, diarrhoea, mucositis) are common after HSCT, resulting in a prolonged hospital stay and increased mortality risk.[23] Patients may experience nausea, vomiting, anorexia and other side effects after pre-treatment, which will lead to insufficient food intake and weight loss,[24] and weight loss is associated with adverse clinical outcomes. Baumgartner et al[14] found that a large amount of weight loss during hospitalization increases bacterial and fungal infection rates in HSCT recipients. However, this study did not find a correlation between high weight loss and pneumonia or sepsis in children, which may be due to the small sample size in this study and the high risk of infection in children after cord blood stem transplantation.[25] Furthermore, high weight loss during hospitalization increased hospitalization and antibiotic costs, which is consistent with the findings of Horsley et al.[26] These clinical outcomes increase the economic burdens imposed on patients' families and health care systems.

Nutritional status is considered an independent and modifiable prognostic risk factor for adverse outcomes.[27] Patients were divided into two groups based on their nutritional status,

Not Proof Read

which was determined by the BMI-Z score at admission.[28] The univariate analyses showed that nutritional status at admission had no significant associations with some short-term clinical outcomes after transplantation, while the multifactorial regression analysis controlling for age, sex and other factors found that malnutrition may increase the risk of liver GVHD. Studies have shown that initial BMI is associated with long-term mortality Nutrition-related laboratory indexes, such as serum albumin and serum total protein, can also affect clinical outcomes. Schaffrath et al analysed 128 allogeneic SCT cases in a retrospective single-centre study and found that serum albumin level (p=0.03) and severe albumin deficiency (p=0.02) strongly correlated with non-relapse mortality at day 30 and day 100.[29] However, this study did not find that the nutritional status on admission had an impact on the one-year mortality or biochemical indexes.

PN, an important nutritional support intervention, has been widely applied in clinical practice. Studies have found that PN can reduce the readmission rate and mortality of patients by improving their nutritional status.[30] However, Takashi et al noted that PN was no more helpful than EN in reducing nutrient-related adverse events in patients receiving HSCT. Some studies have suggested that the use of PN is associated with adverse reactions, such as delayed platelet implantation and an increased infection risk.[31] A meta-analysis showed that EN can reduce the incidence of acute GVHD, specifically grade III-IV and acute gut GVHD. In addition, the indications for and timing of PN remain controversial. Some studies suggest that PN should be routinely used for 15 to 20 days after transplantation or when the patient's oral intake is less than 60% to 70% of the total daily requirement for >3 days.[32] It has also been suggested that the level of albumin before day 8 of preconditioning can be used as a basis for determining whether PN should be applied.[33] The European Society for Parenteral Nutrition believes that PN should be stopped after stem cell implantation according to the patient's condition. The American Society for Parenteral Nutrition also that EN should be administered to transplantation patients with good gastrointestinal function but for whom oral intake fails to meet the total requirement.[34] EN is recommended as first-line nutritional support for patients receiving HSCT by the main international guidelines, but many centres still use PN rather than EN, including our centre, which has a higher PN rate. Nutritional support during the early post-transplantation period for UCBT recipients is an essential and challenging issue. There is no doubt that appropriate nutritional intervention can significantly reduce nutritional deterioration and weight loss in patients after transplantation. Therefore, multiple factors need to be considered in the establishment of optimal nutritional support strategies for different patient groups.

Not Proof Read

There are several limitations to this study. First, as a retrospective study, we collected clinical data from EMRs rather than from direct recordings, which does not guarantee accuracy and accessibility of the data, so the sample size of this study was small. Second, the primary disease of the children included in this study was mainly PID. Generally, the growth and development levels and nutritional status of such paediatric patients are low, so the number of children with obesity was small, and we did not analyse these children in detail, which limited our ability to investigate the effect of obesity on the outcomes. Finally, there may be additional unmeasured confounders at baseline (demographic factors, psychological factors) or different treatments that could be associated with malnutrition, weight loss and poor outcomes.

In conclusion, a large amount of weight loss during the UCBT period was correlated with a high risk of GVHD, longer length of hospitalization and higher total hospitalization cost. Underweight children were more prone to a prolonged PN duration and an increased risk of intestinal GVHD. There was no significant difference in the incidence of other adverse events, ICU transfers or mortality among children with different nutritional statuses. In a larger sample, the differences might be statistically significant. To reduce the incidence of adverse clinical outcomes, financial burdens, and medical resource burdens, nutritional management is urgently needed in paediatric stem cell transplantation wards. Medical staff should provide appropriate nutritional support in a timely manner according to the nutritional status at admission and the weight change during the course of the disease.

ACKNOWLEDGEMENTS

The authors thank the medical and nursing staff at the Department of Hematology and Bone Marrow Transplant Unit of the Children's Hospital of Fudan University. The authors would like to thank all the patients and their carers for participating in this study.

AUTHOR DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Ballen KK, Gluckman E, Broxmeyer HE. Umbilical cord blood transplantation: the first 25 years and beyond. Blood. 2013;122:491-8.

Not Proof Read

2. Gluckman E, Rocha V, Boyer-Chammard A et al. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. N Engl J Med. 1997;337:373-81.
3. Orlando N, Pellegrino C, Valentini CG et al. Umbilical cord blood: Current uses for transfusion and regenerative medicine. Transfus Apher Sci. 2020;59:102952.
4. Kalynychenko TO. Umbilical cord blood banking in the worldwide hematopoietic stem cell transplantation system: perspectives for Ukraine. Exp Oncol. 2017;39:164-170.
5. Sauter C, Abboud M, Jia X et al. Serious infection risk and immune recovery after double-unit cord blood transplantation without antithymocyte globulin. Biol Blood Marrow Transplant. 2011;17:1460-71.
6. Doney K, McMillen K, Buono L, Deeg HJ, Gooley T. Impact of body mass index on outcomes of hematopoietic stem cell transplantation in adults. Biol Blood Marrow Transplant. 2019;25:613-20
7. Lazarow H, Nicolo M, Compher C et al. Nutrition-related outcomes for autologous stem cell transplantation patients. Clin Lymphoma Myeloma Leuk. 2019;19:e393-8.
8. Horsley P, Bauer J, Gallagher B. Poor nutritional status prior to peripheral blood stem cell transplantation is associated with increased length of hospital stay. Bone Marrow Transpl. 2005;35:1113-6.
9. Baumgartner A, Bargetzi A, Zueger N et al. Revisiting nutritional support for allogeneic hematologic stem cell transplantation-a systematic review. Bone Marrow Transplant. 2017;52:506-13.
10. Lazarow H, Singer R, Compher C et al. Effect of malnutrition-driven nutritional support protocol on clinical outcomes in autologous stem cell transplantation patients. Support Care Cancer. 2021;29:997-1003.
11. Paviglianiti A, Dalle JH, Ayas M et al. Low body mass index is associated with increased risk of acute GVHD after umbilical cord blood transplantation in children and young adults with acute leukemia: A Study on Behalf of Eurocord and the EBMT Pediatric Disease Working Party. Biol Blood Marrow Transplant. 2018;24:799-805.
12. Urbain P, Birlinger J, Lambert C et al. Longitudinal follow-up of nutritional status and its influencing factors in adults undergoing allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2013;48:446-51.
13. Fuji S, Einsele H, Savani BN, Kapp M. Systematic nutritional support in allogeneic hematopoietic stem cell transplant recipients. Biol Blood Marrow Transplant. 2015;21:1707-13.
14. Baumgartner A, Zueger N, Bargetzi A et al. Association of nutritional parameters with clinical outcomes in patients with acute myeloid leukemia undergoing haematopoietic stem cell transplantation. Ann Nutr Metab. 2016;69:89-98.
15. Lazarow H, Nicolo M, Compher C et al. Nutrition-related outcomes for autologous stem cell transplantation patients. Clin Lymphoma Myeloma Leuk. 2019;19:e393-8.
16. Thomaz AC, Silvério CI, Campos DJ et al. Pre-transplant arm muscle area: a simple measure to identify patients at risk. Support Care Cancer. 2015;23:3385-91.

Not Proof Read

17. Chen Y, Xu L, Liu D et al. [Increased risk of severe acute graft-versus-host disease in low body mass index patients undergoing haploidentical allogeneic stem cell transplantation]. Zhonghua Nei Ke Za Zhi. 2014;53:710-4
18. Kerby EH, Li Y, Getz KD et al. Nutritional risk factors predict severe acute graft-versus-host disease and early mortality in pediatric allogeneic hematopoietic stem cell transplantation. Pediatr Blood Cancer. 2018;65:
19. Baumgartner A, Zueger N, Bargetzi A et al. Association of nutritional parameters with clinical outcomes in patients with acute myeloid leukemia undergoing haematopoietic stem cell transplantation. Ann Nutr Metab. 2016;69:89-98.
20. Ramachandran V, Kolli SS, Strowd LC. Review of Graft-versus-host disease. Dermatol Clin. 2019;37:569-82.
21. Moreno DF, Cid J. Graft-versus-host disease. Med Clin (Barc). 2019;152:22-8.
22. Aoyama T, Imataki O, Mori K et al. Nutritional risk in allogeneic stem cell transplantation: rationale for a tailored nutritional pathway. Ann Hematol. 2017;96:617-25.
23. Huugen D, Schouten HC, Bos GM. Advantages and limitations of (non-)myeloablative allogeneic stem cell transplantation. Neth J Med. 2002;60:162-9.
24. Fuji S, Einsele H, Savani BN, Kapp M. Systematic nutritional support in allogeneic hematopoietic stem cell transplant recipients. Biol Blood Marrow Transplant. 2015;21:1707-13.
25. Gabelli M, Veys P, Chiesa R. Current status of umbilical cord blood transplantation in children. Brit J Haematol. 2020;190:650-83.
26. HORSLEY P, BAUER J, GALLAGHER B. Poor nutritional status prior to peripheral blood stem cell transplantation is associated with increased length of hospital stay. Bone Marrow Transplant. 2005;35:1113-6.
27. Kranjčec I, Matijašić N, Mašić M et al. Nutritional status as a predictor of adverse events and survival in pediatric autologous stem cell transplant. Pediatr Hemat Oncol. 2020;37:717-31.
28. White JV, Guenter P, Jensen G, Malone A, Schofield M. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). JPEN J Parenter Enteral Nutr. 2012;36:275-83.
29. Schaffrath J, Diederichs T, Unverzagt S et al. Correlation of nutrition-associated parameters with non-relapse mortality in allogeneic hematopoietic stem cell transplantation. Ann Hematol. 2022;101:681-91.
30. Sasabuchi Y, Ono S, Kamoshita S, Tsuda T, Kuroda A. Clinical impact of prescribed doses of nutrients for patients exclusively receiving parenteral nutrition in Japanese hospitals: A retrospective cohort study. JPEN J Parenter Enteral Nutr. 2021;45:1514-22.
31. Sheean PM, Freels SA, Helton WS, Braunschweig CA. Adverse clinical consequences of hyperglycemia from total parenteral nutrition exposure during hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2006;12:656-64.

Not Proof Read

32. Raynard B, Nitenberg G, Gory-Delabaere Get al. [Standards, options and recommendations for nutritional support in bone marrow transplant patients]. Bull Cancer. 2002;89:381-98.
33. Rzepecki P, Barzal J, Sarosiek T, Szczylik C. Biochemical indices for the assessment of nutritional status during hematopoietic stem cell transplantation: are they worth using? A single center experience. Bone Marrow Transplant. 2007;40:567-72.
34. August DA, Huhmann MB. A.S.P.E.N. Clinical guidelines: Nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. Jpen-Parenter Enter. 2009;33:472-500.

Not Proof Read

Table 1. Patient characteristics in different weight loss groups

	All patients (n=91)	Low weight loss (n=67)	High weight loss (n=24)	*p*-value
Age (years)	1.3 (0.8, 3.6)	1.2 (0.7, 2.5)	3.6 (1.9, 6.9)	<0.001
Sex				0.74
Male	78 (85.7)	58 (86.6)	20 (83.3)	
Female	13 (14.3)	9 (13.4)	4 (16.7)	
BMI-Z value at admission				0.025
≤-2	20 (22.0)	18 (26.9)	2 (8.3)	
-2<Z≤-1	12 (13.2)	11 (16.4)	1 (4.2)	
>-1	59 (64.8)	38 (56.7)	21 (87.5)	
Diagnosis				0.003
Primary immunodeficiency disease	83 (91.2)	65 (97.0)	18 (75.0)	
Inflammatory bowel disease	32 (35.2)	22 (32.8)	10 (41.7)	
Severe combined immunodeficiency	22 (24.2)	20 (29.9)	2 (8.3)	
Wiskott-Alarich syndrome	1 (1.1)	1 (1.5)	0 (0.0)	
Chronic granulomatous disease	18 (19.8)	15 (22.4)	3 (12.5)	
Others	10 (11.0)	7 (10.4)	3 (12.5)	
Mucopolysaccharidosis	2 (2.2)	1 (1.5)	1 (4.2)	
Adrenoleukodystrophy	6 (6.6)	1 (1.5)	5 (20.8)	
Albumin at admission (g/L)				
≥35	80 (87.9)	57 (85.1)	23 (95.8)	0.276
<35	11 (12.1)	10 (14.9)	1 (4.2)	
Prealbumin at admission(mg/L)				0.804
≥200	29 (31.9)	22 (32.8)	7 (29.2)	
<200	62 (68.1)	45 (67.2)	17 (70.8)	
Hemoglobin at admission (g/L)				0.104
≥90	83 (91.2)	59 (88.1)	24 (100.0)	
<90	8 (8.8)	8 (11.9)	0 (0.0)	
Time from diagnosis to transplantation (d)	166.0 (62.0, 322.0)	159.0 (59.0, 288.0)	233.0 (101.5, 424.0)	0.167
Time from symptoms to transplantation (d)	392.0 (202.0, 833.0)	358.0 (159.0, 749.0)	562.0 (381.0, 1027.0)	0.031
EN n(%)	41 (45.1)	29 (43.3)	12 (50.0)	0.565

[†]Data are presented as the median (interquartile range) or n (%).

Not Proof Read

Table 2. Differences in clinical outcomes relative to weight loss

Outcomes	Group L † (n=67)	Group H † (n=24)	*p*-value	Univariate OR (95% CI)	Multivariate	
					OR (95% CI)	*p*-value
GVHD n (%)						
Skin GVHD	32 (47.8)	18 (75.0)	0.021	3.281 (1.159-9.292)	5.010 (1.346-18.650)	0.016
Liver GVHD	9 (13.4)	9 (37.5)	0.017	3.867 (1.307-11.437)	3.216(0.411-25.185)	0.266
Intestinal GVHD	3 (4.5)	3 (12.5)	0.185	3.048 (0.571-16.262)	7.269 (1.735-30.448)	0.007
Pneumonia	58 (86.6)	21 (87.5)	1.000	1.086 (0.268-4.399)	1.621 (0.301-8.736)	0.574
Sepsis	17 (25.4)	6 (25.0)	0.971	0.980 (0.334-2.874)	1.733 (0.476-6.303)	0.404
Hypoalbuminemia at discharge	34 (50.7)	5 (20.8)	0.011	0.255 (0.085-0.764)	0.225 (0.064-0.790)	0.020
Low prealbumin at discharge	38 (56.7)	11 (45.8)	0.359	0.646 (0.253-1.648)	0.786 (0.260-2.374)	0.670
Anemia at discharge	25 (37.3)	8 (33.3)	0.728	0.840 (0.314-2.244)	0.678 (0.199-2.302)	0.533
ICU transfers	23 (34.3)	7 (29.2)	0.644	0.788 (0.286-2.172)	1.301 (0.377-4.487)	0.677
One-year mortality	24 (35.8)	4 (16.7)	0.081	2.791 (0.854-9.118)	3.290 (0.820-13.208)	0.093
Time to neutrophil engraftment (d)	19.5 (17.0, 23.5)	21.0 (19.0, 25.5)	0.169			
Time to platelet engraftment (d)	32.0 (25.0, 36.0)	31.0 (29.0, 37.0)	0.597			
PN duration (d)	7 (0, 17)	15 (0, 58)	0.177			
Length of hospitalization (d)	64.5 (46.0, 88.5)	94.0 (65.8, 117.0)	0.004			
Hospitalization costs (million yuan)	26.3 (20.0, 32.0)	37.0 (26.0, 50.2)	0.004			
Antibiotic costs (thousand yuan)	63 (54, 84)	84 (64, 137)	0.008			

Data are presented as median (interquartile range) or n (%).
†Group L represented the low weight loss group, group H represented the high weight loss group.

Not Proof Read

Table 3. Relationship between nutritional status on admission and clinical outcomes

Outcomes	Z >-1 (n=59)	Z ≤-1 (n=32)	*p*-value	Univariate OR (95% CI)	Multivariate	
					OR (95% CI)	*p*-value
GVHD n(%)						
Skin GVHD	35 (59.3)	15 (46.9)	0.254	0.605 (0.254-1.440)	0.827 (0.308-2.217)	0.706
Liver GVHD	10 (16.9)	8 (25.0)	0.357	1.633 (0.571-4.668)	2.533 (0.363-17.677)	0.348
Intestinal GVHD	3 (5.1)	3 (9.4)	0.661	1.931 (0.366-10.176)	3.202 (0.896-11.798)	0.080
Pneumonia	53 (89.8)	26 (81.3)	0.332	0.491 (0.144-1.670)	0.489 (0.124-1.931)	0.307
Sepsis	13 (22.0)	10 (31.3)	0.334	1.608 (0.611-4.236)	1.549 (0.542-4.427)	0.414
Hypoalbuminemia at discharge	24 (40.7)	15 (46.9)	0.568	1.287 (0.541-3.063)	0.868 (0.342-2.207)	0.767
Low prealbumin at discharge	31 (52.5)	18 (56.3)	0.735	1.161 (0.489-2.759)	1.007 (0.399-2.540)	0.988
Anemia at discharge	21 (35.6)	12 (37.5)	0.857	1.086 (0.445-2.650)	0.952 (0.353-2.565)	0.923
ICU transfers	17 (28.8)	13 (40.6)	0.252	1.690 (0.685-4.170)	1.497 (0.540-4.151)	0.438
One-year mortality	17 (28.8)	11 (34.4)	0.583	0.773 (0.307-1.942)	1.066 (0.391-2.909)	0.901
Time to neutrophil engraftment (d)	20 (19,24)	19 (16,24)	0.168			
Time to platelet engraftment (d)	31.0 (26.0,37.0)	34.0 (27.5,35.5)	0.363			
PN duration (d)	3 (0,18)	14 (8,40)	0.008			
Length of hospitalization (d)	73.5 (52.5,101.5)	66.3 (44.5,109.5)	0.826			
Hospitalization costs (million yuan)	26.8 (20.9,35.0)	28.2 (20.3,36.7)	0.842			
Antibiotic costs (thousand yuan)	6.9 (5.6,9.4)	6.4 (5.5,9.5)	0.642			

Data are presented as median (interquartile range) or n (%).

Not Proofread

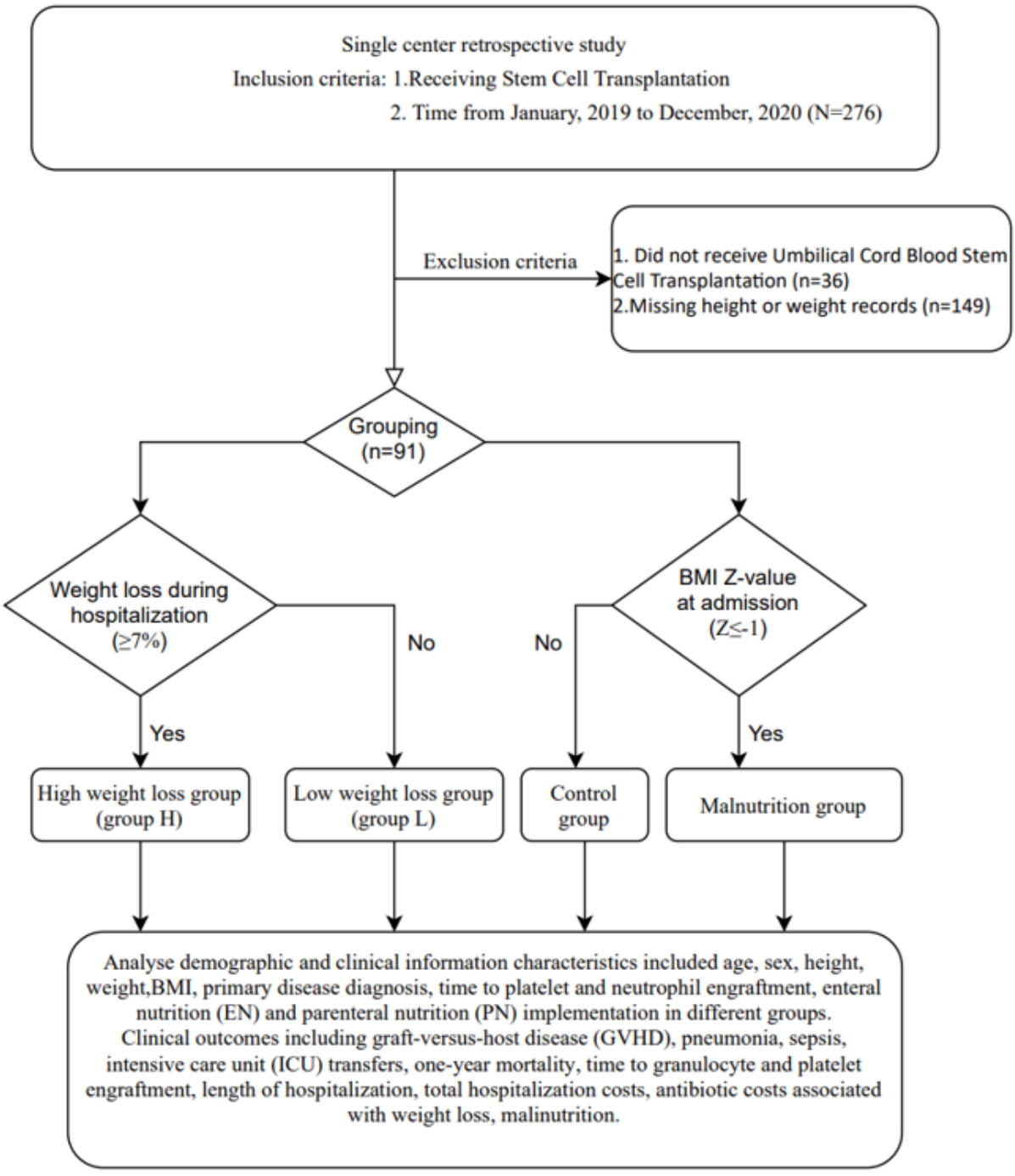

Figure 1. Study design flow chart.