Postprint of a Cohort Study on the Impact of Pre-transplant Skeletal Muscle Mass on Early Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation

Authors: Wu Fangfang, Du Shanshan, Du Xin, Xu Rufu, Sun Aihua, Kong Peiyan, Gao Lei, Zhang Xi, Du Xin

Date: 2023-11-02T00:00:00+00:00

Abstract

Background Allogeneic hematopoietic stem cell transplantation is an effective treatment modality for hematologic malignancies, and malnutrition is a common complication that exerts a negative impact on prognosis. Previous studies have demonstrated that muscle mass can reflect patients' nutritional status earlier than serum biochemical parameters such as albumin, while the impact of pre-transplant muscle mass on early transplant-related complications remains unclear. Objective To investigate the impact of pre-transplant skeletal muscle mass on early outcomes of allogeneic hematopoietic stem cell transplantation, and to provide clinical evidence for implementing nutritional interventions and improving prognosis. Methods This study employed a prospective cohort study design, selecting 77 leukemia patients who underwent allogeneic hematopoietic stem cell transplantation at the Hematology Medical Center of Xinqiao Hospital in Chongqing from January to October 2022 as study subjects. Skeletal muscle mass was assessed using bioelectrical impedance analysis, and patients were divided into a normal skeletal muscle mass group (36 cases) and a low skeletal muscle mass group (41 cases) based on skeletal muscle mass. Baseline data were collected, including personal information and clinical data. SPSS 23.0 software was used to compare oral mucositis, gastrointestinal symptoms, infections, and hematopoietic reconstitution time between the two groups during the early post-transplant period (within 30 days post-transplant). Results The incidence rates of diarrhea, nausea/vomiting, and stomach/abdominal pain showed no statistically significant differences between the normal SMM group and the low SMM group ($P>0.05$). The normal SMM group had lower incidence rates of oral mucositis, hypoalbuminemia, overt gastrointestinal bleeding, and infection compared to the low SMM group ($P<0.05$). The severity of oral

mucositis in the normal SMM group was lower than that in the low SMM group (P<0.001). The neutrophil engraftment time and platelet engraftment time were both longer in the low SMM group than in the normal SMM group (P<0.01). Conclusion The incidence of low skeletal muscle mass in pre-transplant patients is relatively high. Low skeletal muscle mass is associated with the occurrence of oral mucositis, severity of oral mucositis, occurrence of hypoalbuminemia, overt gastrointestinal bleeding, infection, and delayed neutrophil and platelet engraftment during the early post-transplant period. Patients should be screened as early as possible before transplantation, and efforts should be made to actively improve patients' skeletal muscle mass to enhance early transplant outcomes.

Full Text

Title and Authors

Effect of Pre-transplant Skeletal Muscle Mass on Early Outcome of Allogeneic Hematopoietic Stem Cell Transplantation: a Cohort Study

Wu Fangfang[1], Du Shanshan[2], Du Xin[1]*, Xu Rufu[3], Sun Aihua[1], Kong Peiyan[1], Gao Lei[1], Zhang Xi[1]

[1]Medical Center of Hematology, Xinqiao Hospital of Army Medical University, Chongqing 400037, China
[2]Department of Nutritional, Xinqiao Hospital of Army Medical University, Chongqing 400037, China
[3]Department of Pharmacy, Xinqiao Hospital of Army Medical University, Chongqing 400037, China

*Corresponding author: Du Xin, Associate chief nurse; E-mail: 86182681@qq.com

Funding: Chongqing Science and Health Joint Medical Research Project (2023ZDXM022)

Citation: Wu FF, Du SS, Du X, et al. Effect of pre-transplant skeletal muscle mass on early outcome of allogeneic hematopoietic stem cell transplantation: a cohort study[J]. Chinese General Practice, 2023. [Epub ahead of print]. DOI:10.12114/j.issn.1007-9572.2023.0429.

Abstract

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective treatment for hematopoietic malignancies. Malnutrition is a common complication and negatively affects prognosis. Muscle mass has been shown to reflect the nutritional status of patients earlier than blood biochemical parameters such as albumin. However, the influence of pre-transplantation muscle mass on the complications associated with early transplantation remains unclear.

Objective: To investigate the effect of pre-transplant skeletal muscle mass on the early outcomes of allo-HSCT and provide a clinical basis for nutritional interventions and prognosis improvement.

Methods: A prospective cohort study was conducted with 77 leukemia patients who underwent allo-HSCT at the Medical Center of Hematology, Xinqiao Hospital in Chongqing from January to October 2022. Bioelectrical impedance analysis was used to assess skeletal muscle mass. Patients were divided into the normal skeletal muscle mass (normal SMM) group (36 cases) and low skeletal muscle mass (low SMM) group (41 cases) according to their skeletal muscle mass. Baseline data, including personal and clinical details, were collected. Early post-transplant complications (within 30 days post-transplant) such as oral mucositis, gastrointestinal symptoms, infection, and hematopoietic reconstitution time between the two groups were compared using SPSS 23.0 software.

Results: There was no statistically significant difference in the incidence of diarrhea, nausea, vomiting, and abdominal pain/gastritis between the normal and low SMM groups ($P>0.05$). The incidence of oral mucositis, hypoalbuminemia, overt gastrointestinal bleeding, and infection was lower in the normal SMM group than in the low SMM group ($P<0.05$). The severity of oral mucositis in patients in the normal SMM group was lower than that in the low SMM group ($P<0.001$). Neutrophil implantation time and platelet implantation time were longer in patients in the low SMM group than in the normal SMM group ($P<0.01$).

Conclusion: The pre-transplant patients had a high incidence of low skeletal muscle mass. Low skeletal muscle mass before transplantation correlates with the occurrence of oral mucositis, hypoalbuminemia, overt gastrointestinal bleeding, and infections, as well as extended neutrophil and platelet engraftment time in the early transplantation period. Patients should be screened as early as possible prior to transplantation to boost skeletal muscle mass and improve early post-transplant outcomes.

Keywords: Hematopoietic stem cell transplantation; Hematologic diseases; Skeletal muscle mass; Nutritional status; Cohort studies

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective treatment for hematologic malignancies [1]. However, patients undergoing allo-HSCT frequently experience malnutrition due to their underlying disease, prior chemotherapy, and treatment-related toxicities. Pre-transplant malnutrition is associated with adverse clinical outcomes [2-8], and studies have shown that muscle mass reflects nutritional status earlier than blood biochemical parameters such as albumin [9]. The incidence of low skeletal muscle mass (SMM) before transplantation is as high as 62.8% [10], and existing research has confirmed that

pre-transplant skeletal muscle mass is associated with survival outcomes including non-relapse mortality, overall survival, and chronic graft-versus-host disease (cGVHD) [11-13]. Furthermore, some early post-transplant complications such as oral mucositis are related to survival outcomes [14]. Studies have demonstrated that low skeletal muscle content is closely associated with increased incidence of surgical complications and adverse reactions to various anti-tumor treatments in cancer patients [15-17], yet whether pre-transplant skeletal muscle mass affects early transplant-related complications remains unclear. We hypothesized that low pre-transplant skeletal muscle mass may impact early transplant outcomes. Therefore, this prospective cohort study used skeletal muscle mass as the exposure factor to observe its influence on early clinical outcomes, providing a theoretical basis for early nutritional intervention to improve clinical results.

Methods

Study Design and Subjects

Patients with leukemia who underwent allo-HSCT at the Medical Center of Hematology, Xinqiao Hospital in Chongqing between January and October 2022 were selected as study subjects. Inclusion criteria were: (1) diagnosis of leukemia according to established criteria [18-20] and undergoing peripheral blood hematopoietic stem cell transplantation and/or bone marrow transplantation; (2) age 18-65 years; (3) stable condition with clear consciousness and ability to cooperate with all measurements. Exclusion criteria were: (1) severe heart, brain, kidney, or other organ diseases before transplantation; (2) non-first-time allo-HSCT; (3) presence of metal implants such as stents or pacemakers that precluded body composition analysis; (4) pre-existing hypoalbuminemia or diagnosed infection before conditioning. Dropout criteria were: (1) patients whose condition worsened and could not continue participation, those who died during transplantation, or those who refused to participate during follow-up; (2) poor hematopoietic reconstitution during the observation period (within 30 days post-transplant). This study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Army Medical University (approval number: 2022 Research No. 283-01), and all patients provided informed consent.

Sample Size Estimation

Based on the incidence of severe oral mucositis reported in literature [21], with 52.0% in the exposed group and 24.0% in the non-exposed group, and using α=0.05 and β=0.2, the sample size was estimated using the cohort study sample size calculation formula. Considering a 10% dropout rate, 42 cases per group were required, totaling 84 cases for both groups.

Research Methods

This was a prospective cohort study. A self-designed general information questionnaire was used to collect baseline data including gender, age, diagnosis, and

transplant type. Baseline data collection and skeletal muscle mass assessment were completed one day before conditioning. A symptom observation form was established to dynamically record symptoms and hematopoietic reconstitution time daily during the early post-transplant period (within 30 days after transplantation).

1.3.1 Skeletal Muscle Mass Assessment The Inbody S10 device (Biospace, South Korea) was used for body composition analysis based on bioelectrical impedance principles. Measurements were performed in a fasting state after patient admission to the transplant unit but before conditioning. Subjects stood barefoot on the device and held hand electrodes. After entering patient information, body composition analysis results were obtained directly. The standard range for skeletal muscle mass was 90%-110% of the standard skeletal muscle content. Patients with skeletal muscle mass below the lower reference limit were assigned to the low SMM group, while those within the reference range were assigned to the normal SMM group.

1.3.2 Oral Mucositis Evaluated using the World Health Organization (WHO) Oral Mucositis Assessment Scale [22]. The grading criteria were as follows: Grade 0: intact oral mucosa without abnormalities, asymptomatic; Grade I: 1-2 small ulcers with mild erythema and pain, no impact on eating; Grade II: 1-2 large ulcers or multiple small ulcers with increased pain, able to consume semi-liquid foods; Grade III: more than 2 large ulcers with significant pain, able to consume only liquid diet; Grade IV: more than 2 large ulcers or extensive confluent ulcers with severe intolerable pain, unable to eat.

1.3.3 Infection Diagnosed according to the Hospital Infection Diagnostic Criteria issued by the Ministry of Health. HSCT patients with obvious infection foci within 30 days post-transplant, positive blood cultures, positive microbial examination of other specimens such as urine, sputum, or stool, or diagnosis of infection through medical examination were considered infected.

1.3.4 Overt Gastrointestinal Bleeding Defined as hematemesis, melena, or hematochezia [23-24]. The occurrence of overt gastrointestinal bleeding in transplant patients was observed.

1.3.5 Diarrhea Defined as bowel movements significantly exceeding usual frequency (>3 times/day), with loose stools and increased water content (>85%), possibly accompanied by mucus, pus, blood, or undigested food [25].

1.3.6 Nausea and Vomiting Nausea is characterized by retching and/or urgent need to vomit; vomiting is a reflex action of expelling gastric contents through the mouth. Patients reporting nausea and vomiting symptoms were diagnosed accordingly.

1.3.7 Hypoalbuminemia Diagnosed when serum albumin <35 g/L or serum total protein <60 g/L [26].

1.3.8 Stomach Pain/Abdominal Pain Assessed using the Numeric Pain Rating Scale (0-10, where 0 represents no pain and $ $1 indicates pain). Patients reporting pain with confirmation by medical staff of the location in the stomach/abdomen were diagnosed with stomach pain/abdominal pain.

1.3.9 Hematopoietic Reconstitution Time Complete blood count results were monitored to assess hematopoietic reconstitution, primarily including neutrophil engraftment time and platelet engraftment time. Neutrophil (ANC) engraftment was defined as neutrophils exceeding 0.5$×$10^9/L for three consecutive days, with the first day considered as neutrophil engraftment time. Platelet (PLT) engraftment was defined as platelet count $ 20×$10^9/L for seven consecutive days without transfusion support, with the first day of sustained PLT $ 20×$10^9/L considered as platelet engraftment time. Poor hematopoietic reconstitution was defined as ANC or PLT engraftment time exceeding 28 days after stem cell infusion.

Quality Control

(1) Body composition measurements were performed by designated personnel using specified dedicated equipment; (2) Oral mucositis and overt gastrointestinal bleeding were dynamically observed and recorded by designated personnel, while neutrophil engraftment time was obtained by researchers from laboratory results in electronic medical records.

Statistical Analysis

SPSS 23.0 statistical software was used for data analysis. All continuous variables in this study were non-normally distributed and expressed as median (P25, P75). Comparisons between groups were performed using the rank-sum test. Categorical data were analyzed using the 2 test. Comparisons of ordinal data between groups were performed using the Mann-Whitney U test. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics

The study planned to enroll 84 cases. However, 3 cases had poor hematopoietic stem cell engraftment during the observation period, 1 patient refused participation during testing, 1 patient had missing data, and 2 patients had duplicate entries due to basic information input errors. The final sample size included 77 cases, comprising 41 males and 36 females with a median age of 37 (27, 49) years. There were no statistically significant differences between the two groups in age, gender, disease diagnosis, or transplant type ($P>0.05$), as shown in Table 1 .

Table 1 Comparison of baseline data between the two groups

Early Transplant-Related Complications

There were no statistically significant differences in the incidence of diarrhea, nausea/vomiting, or stomach pain/abdominal pain between the normal SMM and low SMM groups (P>0.05). The incidence of oral mucositis, hypoalbuminemia, overt gastrointestinal bleeding, and infection was significantly lower in the normal SMM group compared to the low SMM group (P<0.05), as shown in Table 2 . The severity of oral mucositis in the normal SMM group was significantly lower than that in the low SMM group (Z=6.461, P<0.001), as shown in Table 3 .

Table 2 Comparison of early transplant-related complications between the two groups

Table 3 Comparison of severity of oral mucositis between the two groups

Hematopoietic Reconstitution Time

Neutrophil engraftment time and platelet engraftment time were significantly longer in the low SMM group compared to the normal SMM group (P<0.01), as shown in Table 4 .

Table 4 Comparison of hematopoietic reconstitution between the two groups

Discussion

Patients with malignant leukemia require multiple courses of chemotherapy to achieve disease remission before transplantation, and both chemotherapy and malignant tumors are major contributors to malnutrition. Studies have shown that early assessment of skeletal muscle mass in allo-HSCT patients can provide earlier warning for nutritional intervention [9]. Nutritional screening methods have been reported to predict clinical outcomes [6,27], making pre-transplant nutritional assessment crucial. Various nutritional screening methods are available, and skeletal muscle content has been established as an effective indicator for evaluating malnutrition in cancer patients [28]. Muscle mass reflects nutritional status earlier than blood biochemical parameters such as albumin [9]. Methods for assessing skeletal muscle mass include cross-sectional computed tomography (CT) imaging, dual-energy X-ray absorptiometry, and bioelectrical impedance analysis (BIA). BIA is a mature technique for diagnosing malnutrition that accurately reflects nutritional status with advantages of being simple, rapid, non-invasive, precise, and reliable, and has been applied in nutritional assessment of patients [4]. This study used BIA to assess pre-transplant skeletal muscle mass, revealing a 53.25% incidence of low skeletal muscle mass before transplantation, similar to the 62.8% reported by SHINYA et al. [10]. One

study reported that the prevalence of sarcopenia in adult populations before allo-HSCT was as high as 50.6% [29], indicating that the incidence of low muscle mass before transplantation is relatively high. During malnutrition, protein demand increases significantly, while complications such as infection, gastrointestinal reactions, and mucositis reduce or restrict nutrient intake, exacerbating the risk of malnutrition in transplant patients. Studies have confirmed that malnutrition can lead to delayed hematopoietic reconstitution [38], and our results showed prolonged neutrophil and platelet engraftment times in the low SMM group. This may be because patients in the low SMM group had higher rates of oral mucositis and overt gastrointestinal bleeding, which limit nutrient intake in HSCT patients, worsening malnutrition and consequently delaying hematopoietic reconstitution. However, some studies have reported different findings, suggesting that pre-transplant nutritional parameters are not associated with hematopoietic reconstitution time [39], possibly due to different nutritional assessment indicators used across studies.

Oral mucositis is a common early post-transplant complication. Our results showed that the low SMM group had a higher incidence of oral mucositis and more severe mucositis compared to the normal SMM group, with statistically significant differences. Jiang et al. [21] reported that low muscle mass is associated with the occurrence and severity of gastrointestinal mucositis, consistent with our findings. Studies have shown that in malnourished patients, protein is massively depleted, primarily from muscle albumin consumption, leading to significant muscle loss [30], and our results confirmed a higher incidence of hypoalbuminemia in the low SMM group. The higher incidence and severity of oral mucositis in the low SMM group may be attributed to poorer nutritional status, as nutritional status correlates with mucositis severity—the worse the nutritional status, the more severe the mucositis [33]. This study also demonstrated significantly higher overt gastrointestinal bleeding in the pre-transplant low SMM group. Research has identified platelet count <30$×$10^9/L and pre-transplant gastrointestinal disease or bleeding as important risk factors for gastrointestinal bleeding after haploidentical transplantation [34]; in our study, all gastrointestinal bleeding occurred during the bone marrow suppression period. The cause of overt gastrointestinal bleeding in the low SMM group may be toxic injury to the gastrointestinal mucosa from conditioning chemotherapy, while skeletal muscle is the main protein component in the body that promotes wound repair during acute and chronic disease states [35]. Patients with low muscle mass have low protein content, resulting in slower mucosal repair, which combined with thrombocytopenia during bone marrow suppression, triggers bleeding.

Furthermore, malnutrition is associated with infection. Nutritional status is negatively correlated with nosocomial infection—the poorer the nutritional status, the higher the risk of nosocomial infection [36]. As skeletal muscle content is an effective indicator for assessing malnutrition, our finding of higher infection rates in the low SMM group confirms the relationship between nutrition and infection. Studies have shown that malnutrition affects the quantity and function of immune cells and is associated with immunosuppression, leading to

increased susceptibility to infection [37].

Patients who performed strength exercises and received protein supplementation showed greater relative increase in muscle strength after surgery compared to those receiving protein supplementation alone. Pre-transplant strength training combined with nutritional support can improve muscle mass safely and feasibly [32].

In summary, this study demonstrates that most patients exhibit low skeletal muscle mass before transplantation, with a relatively high incidence. Low skeletal muscle mass affects the occurrence of oral mucositis, severity of mucositis, infection, hypoalbuminemia, and overt gastrointestinal bleeding during early transplantation, and delays neutrophil and platelet engraftment. Low muscle mass patients should be identified early in the clinical course and receive timely intervention to improve clinical outcomes and patient quality of life.

This study has several limitations. First, it is a single-center study with a small sample size, which may limit the generalizability of the findings. Second, the effects of conditioning regimens and the number of reinfused stem cells were not evaluated, preventing comprehensive analysis of the impact of skeletal muscle mass on early transplant outcomes. Therefore, future studies are needed to clarify the relationship between pre-transplant skeletal muscle mass and early transplant-related complications.

Author Contributions

Wu Fangfang was responsible for drafting the manuscript, literature review, proposing research ideas, and final revision; Du Shanshan was responsible for data collection; Du Xin was responsible for creating figures and tables and providing guidance on manuscript revision; Xu Rufu was responsible for statistical guidance, including sample size calculation and statistical analysis; Sun Aihua was responsible for literature review; Kong Peiyan was responsible for study implementation and enrolling eligible patients; Gao Lei was responsible for study implementation and enrolling eligible patients; Zhang Xi was responsible for study design and proposing inclusion of secondary observation indicators such as diarrhea, nausea/vomiting, hypoalbuminemia, and platelet engraftment time.

Conflict of Interest: This article has no conflict of interest.

References

[1] WANG X Q, HUANG R H, ZHANG X H, et al. Current status and prospects of hematopoietic stem cell transplantation in China[J]. Chin Med J, 2022, 135(12): 1394-1403. DOI:10.1097/CM9.0000000000002235.

[2] BAUMGARTNER A, BARGETZI A, ZUEGER N, et al. Revisiting nutritional support for allogeneic hematologic stem cell transplantation-a systematic review[J]. Bone Marrow Transplant, 2017, 52(4): 506-513.

DOI:10.1038/bmt.2016.310.

[3] ARAIE H, KAWAGUCHI Y, OKABE M, et al. Prediction of clinical outcome by controlling nutritional status (CONUT) before allogeneic hematopoietic stem cell transplantation in myeloid malignancies[J]. Int J Hematol, 2019, 110(5): 599-605. DOI:10.1007/s12185-019-02723-w.

[4] TAMAKI M, NAKASONE H, NAKAMURA Y, et al. Body weight loss before allogeneic hematopoietic stem cell transplantation predicts survival outcomes in acute leukemia patients[J]. Transplant Cell Ther, 2021, 27(4): 340.e1-340.e6. DOI:10.1016/j.jtct.2021.01.006.

[5] EGLSEER D, BAUER S, HUBER-KRAßNITZER B, et al. Malnutrition risk prior to hematopoietic stem cell transplantation predicts mortality in adults[J]. Bone Marrow Transplant, 2021, 56(9): 2268-2271. DOI:10.1038/s41409-021-01292-z.

[6] HIROSE E Y, DE MOLLA V C, GONÇALVES M V, et al. The impact of pretransplant malnutrition on allogeneic hematopoietic stem cell transplantation outcomes[J]. Clin Nutr ESPEN, 2019, 33: 213-219. DOI:10.1016/j.clnesp.2019.05.005.

[7] ORVAIN C, BYELYKH M, OTHUS M, et al. Relationship between pretransplantation nutritional status and outcome in adults with acute myelogenous leukemia undergoing allogeneic hematopoietic cell transplantation[J]. Transplant Cell Ther, 2022, 28(12): 846.e1-846.e9. DOI:10.1016/j.jtct.2022.09.023.

[8] SIVGIN S, BALDANE S, OZENMIS T, et al. The impact of pretransplant hypoalbuminemia on survival in patients with leukemia who underwent allogeneic hematopoietic stem cell transplantation (alloHSCT): a nutritional problem?[J]. Transplant Proc, 2013, 45(9): 3371-3374. DOI:10.1016/j.transproceed.2013.02.144.

[9] ZHANG W J, MA L F, WANG Z M, et al. Investigation of limb muscle mass and its influencing factors in patients undergoing allogeneic hematopoietic stem cell transplantation[J]. Chinese Journal of Tissue Engineering Research, 2021, 25(13): 1999-2004.

[10] YOSHIDA S, SAKURAI G, YAHATA T. Prevalence of low skeletal muscle quantity and quality and their associated factors in patients before allogeneic hematopoietic stem cell transplantation[J]. Intern Emerg Med, 2022, 17(2): 451-456. DOI:10.1007/s11739-021-02828-3.

[11] SAKATOKU K, ITO A, TAJIMA K, et al. Prognostic significance of low pre-transplant skeletal muscle mass on survival outcomes in patients undergoing hematopoietic stem cell transplantation[J]. Int J Hematol, 2020, 111(2): 267-277. DOI:10.1007/s12185-019-02723-w.

[12] RIER H N, KHARAGJITSING H, VAN ROSMALEN J, et al. Prognostic impact of low muscle mass and low muscle density in patients with diffuse large

B-cell lymphoma[J]. Leuk Lymphoma, 2020, 61(5): 10428194.2020.1737686. DOI:10.1080/10428194.2020.1737686.

[13] LJUBAS KELECIC D, LELAS A, KARAS I, et al. Sarcopenia among patients after allogeneic hematopoietic stem cell transplantation and the impact of chronic graft-versus-host disease[J]. J Cancer Res Clin Oncol, 2020, 146(11): 2967-2978. DOI:10.1007/s00432-020-03280-0.

[14] VERA-LLONCH M, OSTER G, FORD C M, et al. Oral mucositis and outcomes of allogeneic hematopoietic stem-cell transplantation in patients with hematologic malignancies[J]. Support Care Cancer, 2007, 15(5): 491-496. DOI:10.1007/s00520-006-0149-5.

[15] KUBO Y, NAITO T, MORI K, et al. Skeletal muscle loss and prognosis of breast cancer patients[J]. Support Care Cancer, 2017, 25(7): 2221-2227. DOI:10.1007/s00520-017-3628-7.

[16] OKUMURA S, KAIDO T, HAMAGUCHI Y, et al. Impact of the preoperative quantity and quality of skeletal muscle on outcomes after resection of extrahepatic biliary malignancies[J]. Surgery, 2016, 159(3): 821-833. DOI:10.1016/j.surg.2015.08.047.

[17] SHACHAR S S, WILLIAMS G R, MUSS H B, et al. Prognostic value of sarcopenia in adults with solid tumours: a meta-analysis and systematic review[J]. Eur J Cancer, 2016, 57: 58-67. DOI:10.1016/j.ejca.2015.12.030.

[18] Leukemia and Lymphoma Group, Chinese Society of Hematology, Chinese Medical Association. Guidelines for the diagnosis and treatment of adult acute myeloid leukemia (not acute promyelocytic leukemia) in China (2021 edition)[J]. Chinese Journal of Hematology, 2021, 42(8): 617-623. DOI:10.3760/cma.j.issn.0253-2727.2021.08.001.

[19] Hematology Oncology Committee of China Anti-Cancer Association, Leukemia and Lymphoma Group, Chinese Society of Hematology, Chinese Medical Association, QIU L G, et al. Guidelines for the diagnosis and treatment of adult acute lymphoblastic leukemia in China (2021 edition)[J]. Chinese Journal of Hematology, 2021, 42(9): 705-716.

[20] Leukemia and Lymphoma Group, Chinese Society of Hematology, Chinese Medical Association, XIAO Z J. Chinese guidelines for the diagnosis and treatment of chronic myelomonocytic leukemia (2021 edition)[J]. Chinese Journal of Hematology, 2021, 42(1): 5-9.

[21] JIANG S S, XUE S L, GE Y Q, et al. Relationship between nutritional indicators and early clinical outcomes in patients undergoing hematopoietic stem cell transplantation[J]. Cancer Progress, 2022, 20(2): 130-134, 165.

[22] QUINN B, POTTING C M J, STONE R, et al. Guidelines for the assessment of oral mucositis in adult chemotherapy, radiotherapy and haematopoietic stem cell transplant patients[J]. Eur J Cancer, 2008, 44(1): 61-72. DOI:10.1016/j.ejca.2007.09.014.

[23] AWADIE H, ZOABI A, GRALNEK I M. Obscure-overt gastrointestinal bleeding: a review[J]. Pol Arch Intern Med, 2022, 132(5): 16253. DOI:10.20452/pamw.16253.

[24] RAMOS G P, BINDER M, HAMPEL P, et al. Outcomes of endoscopic intervention for overt GI bleeding in severe thrombocytopenia[J]. Gastrointest Endosc, 2018, 88(1): 55-61. DOI:10.1016/j.gie.2018.01.028.

[25] WU K C, ZOU D W. Guidelines for primary care diagnosis and treatment of chronic diarrhea (practice version · 2019)[J]. Chinese Journal of General Practitioners, 2020, 19(11): 983-989.

[26] NICHOLSON J P, WOLMARANS M R, PARK G R. The role of albumin in critical illness[J]. Br J Anaesth, 2000, 85(4): 599-610. DOI:10.1093/bja/85.4.599.

[27] IESTRA J A, FIBBE W E, ZWINDERMAN A H, et al. Body weight recovery, eating difficulties and compliance with dietary advice in the first year after stem cell transplantation: a prospective study[J]. Bone Marrow Transplant, 2002, 29(5): 417-424. DOI:10.1038/sj.bmt.1703375.

[28] Chinese Society for Parenteral and Enteral Nutrition. Guidelines for nutritional support in cancer patients[J]. Chinese Journal of Surgery, 2017, 55(11): 801-829. DOI:10.3760/cma.j.issn.0529-5815.2017.11.001.

[29] MORISHITA S, KAIDA K, TANAKA T, et al. Prevalence of sarcopenia and relevance of body composition, physiological function, fatigue, and health-related quality of life in patients before allogeneic hematopoietic stem cell transplantation[J]. Support Care Cancer, 2012, 20(12): 3161-3168. DOI:10.1007/s00520-012-1460-5.

[30] REN G X, LI M H, YU C R, et al. Nutritional status and ECOG score in patients after hematopoietic stem cell transplantation[J]. China Medical Herald, 2017, 14(35): 125-128.

[31] PIERIK V D, MESKERS C G M, VAN ANCUM J M, et al. High risk of malnutrition is associated with low muscle mass in older hospitalized patients - a prospective cohort study[J]. BMC Geriatr, 2017, 17(1): 118. DOI:10.1186/s12877-017-0491-5.

[32] RUPNIK E, SKERGET M, SEVER M, et al. Feasibility and safety of exercise training and nutritional support prior to haematopoietic stem cell transplantation in patients with haematological malignancies[J]. BMC Cancer, 2020, 20(1): 1142. DOI:10.1186/s12885-020-07637-z.

[33] KRAWCZYK J, KRAJ L, KORTA T, et al. Nutritional status of hematological patients before hematopoietic stem cell transplantation and in early posttransplantation period[J]. Nutr Cancer, 2017, 69(8): 1205-1210. DOI:10.1080/01635581.2017.1367937.

[34] SUN X Y, SU Y, LIU X, et al. Overt gastrointestinal bleeding following

haploidentical haematopoietic stem cell transplantation: incidence, outcomes and predictive models[J]. Bone Marrow Transplant, 2021, 56(6): 1341-1351. DOI:10.1038/s41409-021-01267-0.

[35] RIBEIRO S M L, KEHAYIAS J J. Sarcopenia and the analysis of body composition[J]. Adv Nutr, 2014, 5(3): 260-267. DOI:10.3945/an.113.005256.

[36] LIN J L. Study on the correlation between nutritional status and nosocomial infection in children with acute lymphoblastic leukemia[D]. Hefei: Anhui Medical University, 2020.

[37] ALWARAWRAH Y, KIERNAN K, MACIVER N J. Changes in nutritional status impact immune cell metabolism and function[J]. Front Immunol, 2018, 9: 1055. DOI:10.3389/fimmu.2018.01055.

[38] SONG N, ZHOU X. Nutritional status and its relationship with hematopoietic reconstitution in children undergoing hematopoietic stem cell transplantation[J]. Chinese Journal of Applied Clinical Pediatrics, 2016, 31(16): 1255-1258. DOI:10.3760/cma.j.issn.2095-428X.2016.16.016.

[39] ESPINOZA M, PERELLI J, OLMOS R, et al. Nutritional assessment as predictor of complications after hematopoietic stem cell transplantation[J]. Rev Bras Hematol Hemoter, 2016, 38(1): 7-14. DOI:10.1016/j.bjhh.2015.10.002.

Note: Figure translations are in progress. See original paper for figures.