Original Article

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Nutritional status impact on engraftment time in hematopoietic stem cell transplants (HSCT) in Semarang, Indonesia: A cross-sectional study

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Abstract

Background: Nutritional support is a critical consideration in the care of individuals undergoing hematopoietic stem cell transplantation (HSCT), given the metabolic alterations induced by intensive treatments. This study aimed to explore the correlation between nutritional status and the time to engraftment in HSCT patients at Dr. Kariadi General Hospital, Semarang, Indonesia.

Methods: This study included adult patients with malignant diseases who underwent autologous or allogeneic HSCT at Dr. Kariadi General Hospital between 2013 and 2023. Nutritional status was evaluated using body mass index (BMI), energy intake, and the type and duration of nutritional support. Neutrophil and platelet engraftment were defined as the time to sustained absolute neutrophil count (ANC) ≥500 cells/mm³ and platelet count ≥20 × 10⁹/L, respectively, and correlations between numerical variables were analyzed using Pearson's test.

Results: A total of 45 HSCT patients were involved in this study. There was a significant negative correlation between nutritional intake and neutrophil engraftment (r = -0.776, p <0.001) and platelet engraftment (r= -0.72, P = 0.00), indicating that as the engraftment time increased, nutritional intake decreased. Furthermore, a positive but weak correlation (r = 0.24, P = 0.10) was found between BMI and time to engraftment.

Conclusion: The study highlights that nutritional status significantly influences engraftment time in HSCT patients, supporting the importance of comprehensive nutritional support to improve outcomes and shorten engraftment.

Keywords: Hematopoietic stem cell transplantation, Nutritional status, Engraftment time, Body mass index, Energy intake.

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Idiopathic Nutritional assistance stands as a paramount concern in the care of individuals undergoing hematopoietic stem cell transplantation (HSCT). Numerous factors contribute to metabolic alterations during HSCT, encompassing the impact of intensive chemotherapy and whole-body irradiation, mucositis resulting in painful ulcers, reduced food intake, as well as occurrences of nausea, vomiting, and diarrhea.1 Among the various types of HSCT, allogeneic HSCT (allo-HSCT) typically instigates the most profound shifts in body composition and muscle metabolism, accompanied by challenges such as infections and the onset of acute graft-versus-host disease (GVHD) (1, 2). Other metabolic consequences related to cancer diagnoses, such as cachexia, contribute to the onset of malnutrition, alongside the decrease in nutritional intake resulting from diverse therapeutic side effects (3).

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Reports indicate that malnutrition is commonly observed in 40-80% of cancer patients, with various research findings emphasizing malnutrition as a primary factor linked to elevated infection rates, increased morbidity and mortality, prolonged hospital stays, and heightened medical costs in this patient population (3). Additionally, research outcomes highlight the association between malnutrition, extended hospitalization, and elevated mortality risk in hematopoietic stem cell transplantation patients, underscoring a correlation between poor prognosis and severe GVHD (4).

The study by Hadjibabaie et al. also found that pre-engraftment BMI influences the time to engraftment in patients undergoing HSCT. However, current data on this topic remain very limited, particularly in Asian populations and in Indonesia (5, 6). Nutrition is a form of supportive care designed to sustain patients' nutritional well-being throughout the transplant procedure. This study aimed to elucidate the intricate correlation between nutritional status and the time to engraftment in patients undergoing HSCT procedures in Semarang, Indonesia.

Methods

Patients: A total of 45 participants involved in this study comprised adult individuals with malignant diseases who underwent autologous and allogenic HSCT procedures at Dr. Kariadi General Hospital Semarang, Indonesia. Informed consent was obtained from all of the patients. Medical records were used to find the data of the variables. This study has been approved by the Ethics Committee of Dr. Kariadi General Hospital with number 1488/EC/KEPK/-RSDK/2023.

Inclusion and exclusion criteria: Inclusion criteria included adults (age ≥ 18 years) with a confirmed indication for HSCT from 2013-2023. Exclusion criteria involved individuals with pre-existing malabsorption disorders or those with incomplete medical record data.

Transplant procedure: All HSCT procedures adhered to standard protocols established at the Dr. Kariadi General Hospital, Semarang, Indonesia. This included the type of engraftment (autologous transplant or allogenic transplant) and the diagnosis of the disease that needs the transplant procedure.

Definition

Body Mass Index (BMI): BMI was calculated using the standard formula by the World Health Organization (WHO) classification: BMI = weight (kg) / (height (m^2) (7). Individuals with a BMI below 18.5 kg/m^2 are considered underweight, 18.5 kg/m^2 to 24.9 kg/m^2 were categorized as normal weight, 25 kg/m^2 to 29.9 kg/m^2 as overweight, and above 30 kg/m^2 as obese. BMI was measured prior to undergoing HSCT.

Energy intake: Energy intake represents the quantifiable measure of the energy content obtained from macronutrients such as carbohydrates, proteins, and fats, as well as other sources like alcohol. Energy intake was measured by the nutritionist. Daily intake of energy and protein was calculated using Food Processor software. The Food Processor software was utilized to determine the daily energy and protein intake. The energy needs of patients before hematopoietic stem cell transplantation (HSCT) were computed as 1.4 times the basal metabolic rate (BMR). The BMRs were estimated using the Harris-Benedict equation (8).

Time to engraftment: The time to engraftment was defined as the number of days from stem cell infusion to the first sustained increase in absolute neutrophil count (ANC) to ≥500 cells/mm³. The European Society for Blood and Marrow Transplantation (EBMT) criteria for neutrophil engraftment in the context of hematopoietic stem cell transplantation typically involve the first day of achieving a sustained ANC equal to or exceeding a specific threshold, commonly set at $\geq 0.5 \times 10^9$ cells/L (9). This sustained recovery signifies the successful engraftment of donor neutrophils into the recipient's bloodstream. Similarly, platelet engraftment is defined as the initial day of attaining a sustained platelet count meeting or surpassing a specified threshold, often established at $\geq 20 \times 10^9$ cells/L. This achievement occurs without the need for transfusion support and marks a crucial milestone in the post-transplantation period, indicating the successful integration of donor cells and the commencement of hematopoietic recovery.

Statistical analysis: Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) 25 version. Descriptive statistics were utilized to provide a comprehensive overview of the demographic and clinical characteristics of the study population. Categorical data were presented using percentages, while numerical data were reported using the mean and standard deviation. The correlation between nutritional parameters, such as nutritional intake and time to engraftment was evaluated using suitable statistical tests. The Pearson correlation test was used to find the correlation between numerical variables. Statistical significance was set at $p < 0.05$ with a confidence interval of 95%.

Ethical clearance: Ethical approval was obtained from the Ethics Committee of Dr. Kariadi General Hospital in Semarang, Indonesia, before the commencement of the study (No. 1487/EC/KEPK-RSDK/2023).

Results

Characteristics of patients and the HSCT procedure: This study involved 45 HSCT patients, with an average age of 37.07 years and a standard deviation of 10.34. The baseline of characteristics is provided in table 1. Gender distribution among the participants consisted of 24 (53%) males and 21 (47%) females. The time required for neutrophil engraftment ranged from 10 to 21 days, averaging approximately 14.29 days with a standard deviation of 3.32. Meanwhile the platelet engraftment had a mean on 13.53 days with 3.09 standard deviation. HSCT procedures included 7 (16%) allogeneic and 38 (84%) autologous transplantations. Disease diagnoses encompassed 1 (2%) case of acute lymphoblastic leukemia (ALL), 7 (16%) cases of acute myeloid leukemia (AML), 6 (13%) cases of Hodgkin's lymphoma, 3 (7%) cases of non-Hodgkin's lymphoma, 1 (2%) case of Mixed-Phenotype Acute Leukemia (MPAL), and 27 (60%) cases of multiple myeloma.

Nutritional status of the HSCT patients: The types of nutrition provided to the participants in this study included 24 (60%) individuals receiving oral nutrition and 16 (40%) patients receiving parenteral nutrition. The duration of nutrition received by the participants varied from 14 to 30 days, with an average duration of approximately 20.86 days and a standard deviation of 4.34 days (table 2). The mean BMI for the group was approximately 23.47, with a standard deviation of 2.72. Approximately 8 (18%) of the population was classified as underweight, indicating a lower-than-normal body weight. Nearly half of the individuals, around 21 (47%) fall within the normal BMI range, suggesting a healthy weight status. About 11 (24%) of the population was considered overweight, signifying an excess of body weight. Furthermore, approximately 5 (11%) of individuals were classified as obese.

Table 1. Baseline characteristics

Characteristics	
Gender (n, %)	
Male	24 (53%)
Female	21 (47%)
Age (mean±SD)	37.07 years±10.34
Type of Transplant (n, %)	
Autologous	38 (84%)
Allogenic	7 (16%)
Neutrophil Engraftment (mean±SD)	14.29 days±3.32
Platelet Engraftment (mean±SD)	13.53 days±3.09
Diagnosis (n, %)	
ALL	1 (2%)
AML	7 (16%)
Hodgkin's lymphoma	6 (13%)
Non-Hodgkin's lymphoma	3 (7%)
MPAL	1 (2%)
Multiple myeloma	27 (60%)

*ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, MPAL: Mixed-Phenotype Acute Leukemia

Table 2. Nutritional status of HSCT patients

Nutritional status	
Type of nutrition	
Oral	24 (60%)
Parenteral	16 (40%)
Duration of nutrition	20.86 days±4.34
BMI	
Underweight	8 (18%)
Normal	21 (47%)
Overweight	11 (24%)
Obese	5 (11%)

Correlation between nutritional status and time to engraftment in HSCT procedure patients: The results indicate significant associations between neutrophil engraftment and nutritional intake, with a Pearson correlation coefficient of -0.776 (p <0.001). This negative correlation suggests that as the neutrophil engraftment increases, there was a corresponding decrease in nutritional intake (figure 1). The Pearson correlation results between energy intake and platelet engraftment yielded a correlation coefficient of -0.72 with a p value of 0.00. This outcome suggests that as patients' energy intake undergoing HSCT increases, the time taken to achieve platelet engraftment decreases (figure 2). The results revealed a Pearson correlation coefficient of 0.24 between time to engraftment and BMI, with a corresponding a p-value of 0.10. This correlation suggests a positive but relatively weak association between the total time of exercise and BMI (figure 3).

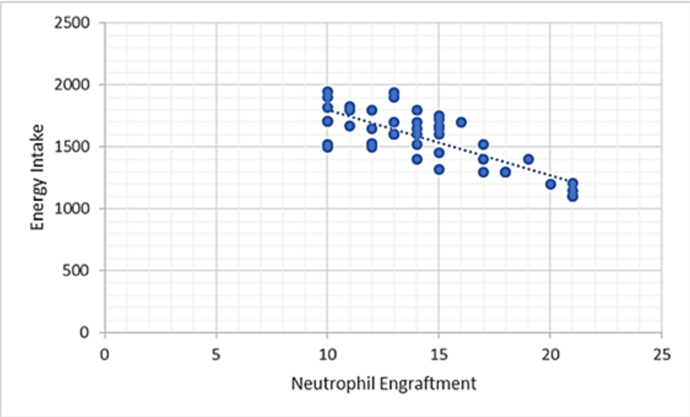

Figure 1. Correlation between energy intake and neutrophil engraftment

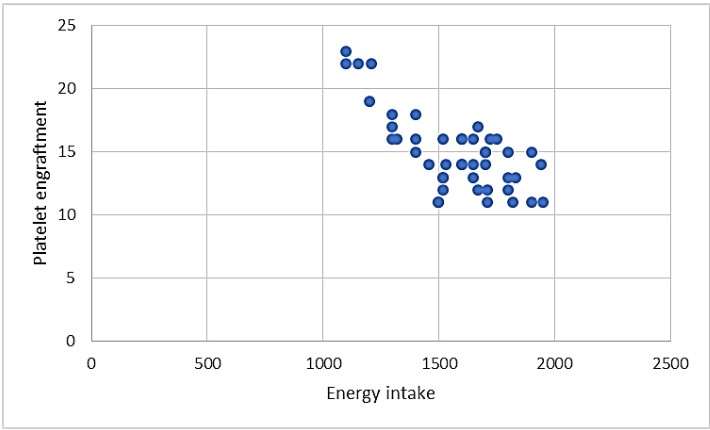

Figure 2. Correlation between energy intake and platelet engraftment

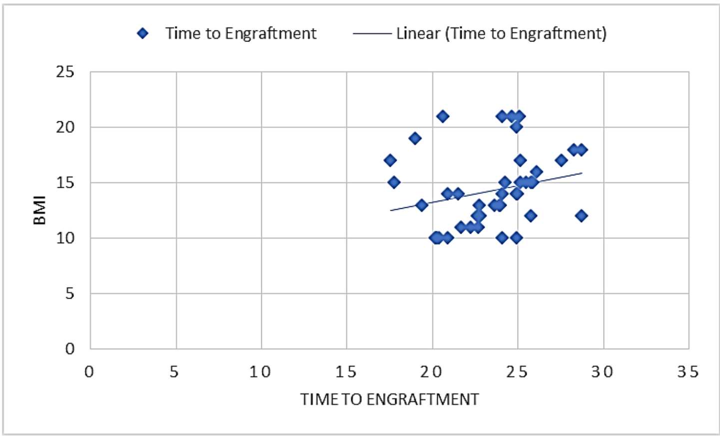

Figure 3. Correlation between BMI and time to engraftment

Discussion

HSCT represents a notably demanding state, necessitating elevated energy expenditure due to a hypermetabolic condition. This state is characterized by escalated rates of both breakdown (catabolism) and synthesis (anabolism), arising from cytoreductive therapy and complications like infections, multiple organ failure, and tissue healing (10). Additionally, the widely accepted approach of high-dose conditioning in the treatment of hematological malignancies can lead to considerable gastrotoxicity and nutrition-related symptoms. Post-transplantation, weight loss is frequently documented, underscoring the physiological challenges and impact on nutritional status associated with HSCT (11). In this research, we observed an inverse correlation between nutritional intake and the time required for engraftment in patients undergoing HSCT procedure. We also found a positive correlation between BMI and time to engraftment in HSCT patients. This implies that nutrition plays a role in determining the timeframe for achieving engraftment. Previous literature lacks comprehensive documentation regarding the nutritional status of patients during HSCT, and diverse methods have been employed to assess this status. For instance, a study involving 100 HSCT patients indicated that they were either at or above their ideal body weight, with none experiencing significant weight reduction (less than 10%) in the preceding 6 months (12).

Conversely, another study reported that 73% of patients were adequately nourished, 23% exhibited moderate malnutrition or were at risk of malnutrition, and 4% were severely malnourished (13). Several studies, including the one conducted by Hadjibabaie et al., have highlighted the potential impact of pre-engraftment BMI on the time to engraftment in patients undergoing HSCT. A lower or higher than normal BMI may influence various physiological factors, such as immune recovery, nutritional status, and the bone marrow microenvironment, all of which can affect the engraftment process. Patients with suboptimal BMI may experience delayed hematologic recovery, increasing their risk for complications such as infections and prolonged hospital stays (6). The impact of nutritional status on the time to engraftment in patients undergoing HSCT is a complex interplay of physiological processes. Nutritional status, reflecting the intake of vital nutrients, plays a pivotal role in supporting the intricate mechanisms involved in the engraftment phase of HSCT. Essential for cellular proliferation, nutrients such as amino acids, vitamins, and minerals contribute to DNA synthesis and cell division, critical processes during engraftment. Moreover, the immune system, fundamental in preventing infections and graft rejection, depends on proper nutrition for optimal functioning (14). Nutrition also plays a crucial role in the success of cell transplantation through several biological mechanisms. Adequate nutritional status supports immune function, tissue repair, and hematopoiesis, all of which are essential for effective engraftment and recovery. Specific nutrients, such as proteins, vitamins, and trace elements, are involved in cellular proliferation, antioxidant defense, and modulation of inflammatory responses, which can influence transplant outcomes. Malnutrition or imbalances in body composition may impair these processes, leading to delayed engraftment, increased susceptibility to infections, and poorer overall prognosis. Therefore, optimizing nutritional status before and after transplantation is critical to enhance biological readiness and support recovery (15-16). Malnutrition may compromise immune responses, potentially leading to delayed engraftment. HSCT induces a hypermetabolic state with increased energy demands, and nutritional intake provides the necessary energy substrates for cellular processes.[15] Gastrotoxicity from high-dose conditioning regimens can impede nutritional intake due to symptoms such as nausea and vomiting, affecting the body's recovery and potentially prolonging engraftment. Additionally, the nutritional status' close ties to body composition, including muscle mass and fat stores, underscore the importance of adequate nutrient reserves for post-transplant recovery. The intricate correlation between nutritional status and time to engraftment in HSCT patients involves supplying essential nutrients for cellular processes, meeting energy demands, supporting immune function, and mitigating complications (16-19).

Ensuring optimal nutritional support emerges as a crucial factor in improving outcomes and minimizing the duration required for successful engraftment in HSCT patients (20). This study was conducted at a single center, which may limit the generalizability of the findings due to potential variations in patient characteristics and clinical practices across different institutions. To obtain more representative results, future multicenter studies are recommended. Additionally, body composition was measured after HSCT to ensure more accurate assessments by minimizing the influence of acute changes related to the transplant process. In this study, we observed a negative correlation between the intake of nutrients and the duration of engraftment in patients undergoing HSCT. The correlation between nutritional intake and the time required for engraftment in HSCT patients is a multifaceted interplay of physiological processes. Nutritional status, reflective of the ingestion of essential nutrients, plays a crucial role in supporting the intricate mechanisms involved in the engraftment phase of HSCT.

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Conflict of interests: There was no conflict of interest in this study.

Authors' contribution: All authors contributed equally in this research.

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