Theoretical Construction and Expert Validation of a Nutritional Protocol for Hematopoietic Stem Cell Transplantation: Early Enteral Nutrition Therapy

https://doi.org/10.32635/2176-9745.RBC.2025v71n4.5354EN

Construção Teórica e Validação por Especialistas de um Protocolo Nutricional para o Transplante de Células-Tronco Hematopoiéticas: Terapia Nutricional Enteral Precoce

Construcción Teórica y Validación por Expertos de un Protocolo Nutricional para el Trasplante de Células Madre Hematopoyéticas: Terapia Nutricional Enteral Temprana

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ABSTRACT

Introduction: This study addresses the development and validation of a nutritional protocol aiming to systematize early enteral nutritional therapy for patients of the Bone Marrow Transplant Service at a university hospital in Fortaleza, Ceará. **Objective:** To develop and validate, based on evidence and expert opinions, a nutritional protocol focused on early enteral therapy in hematopoietic stem cell transplantation. **Method:** Methodological study divided into two phases. The first consisted of gathering scientific evidence through an integrative literature review, conducted in the PubMed and LILACS databases, using Portuguese and English descriptors combined with the Boolean operators AND and OR. After applying the eligibility criteria, 27 articles were selected to support the protocol construction. In the second phase, the protocol was submitted to evaluation by 11 specialists with experience in clinical nutrition, onco-hematology, oncology, and/or enteral nutritional therapy, through a structured questionnaire with a Likert-type scale. Agreement among judges was analyzed using the Content Validity Index (CVI), considering 0.80 as the minimum acceptable value. **Results:** The protocol obtained a global CVI of 0.87, indicating good content validity. **Conclusion:** The protocol presents content validated by experts, representing a potential tool for clinical practice. However, the need for validation with end users to confirm its applicability is emphasized.

Key words: Clinical Protocols/standards; Enteral Nutrition/standards; Hematopoietic Stem Cell Transplantation; Hematologic Neoplasms/diet therapy.

RESUMO

Introdução: Este estudo trata da construção e validação de um protocolo nutricional, buscando sistematizar a terapia nutricional enteral precoce, destinado a pacientes do Serviço de Transplante de Medula Óssea de um hospital universitário em Fortaleza, Ceará. **Objetivo:** Construir e validar, com base em evidências e pareceres de especialistas, um protocolo nutricional voltado à terapia enteral precoce no transplante de células-tronco hematopoiéticas. **Método:** Pesquisa metodológica dividida em duas fases. A primeira consistiu no levantamento de evidências científicas, por meio de uma revisão integrativa da literatura, realizada nas bases PubMed e LILACS, utilizando descritores em português e inglês, combinados pelos operadores booleanos AND e OR. Após aplicação dos critérios de elegibilidade, 27 artigos foram utilizados para embasar a construção do protocolo. Na segunda fase, o protocolo foi submetido à avaliação de 11 especialistas com experiência em nutrição clínica, onco-hematologia, oncologia e/ou terapia nutricional enteral, por meio de um questionário estruturado com escala do tipo Likert. A análise da concordância entre os juízes foi realizada por meio do Índice de Validade de Conteúdo (IVC), considerando-se como valor mínimo aceitável 0,80. **Resultados:** O protocolo obteve um IVC global de 0,87, demonstrando boa validade de conteúdo. **Conclusão:** O protocolo apresenta conteúdo validado por especialistas, representando uma ferramenta potencial para a prática clínica. Ainda assim, destaca-se a importância de sua validação com os usuários finais para confirmação de aplicabilidade.

Palavras-chave: Protocolos Clínicos/normas; Nutrição Enteral/normas; Transplante de Células-Tronco Hematopoéticas; Neoplasias Hematológicas/dietoterapia.

RESUMEN

Introducción: Este estudio aborda la elaboración y validación de un protocolo nutricional con el objetivo de sistematizar la terapia nutricional enteral temprana, destinado a pacientes del Servicio de Trasplante de Médula Ósea de un hospital universitario en Fortaleza – Ceará. **Objetivo:** Construir y validar, con base en evidencias y en opiniones de especialistas, un protocolo nutricional enfocado en la terapia enteral temprana en el trasplante de células madre hematopoyéticas. **Método:** Estudio metodológico dividido en dos fases. La primera consistió en el levantamiento de evidencias científicas mediante una revisión integradora de la literatura, realizada en las bases de datos PubMed y LILACS, utilizando descriptores en portugués e inglés combinados con los operadores booleanos AND y OR. Tras aplicar los criterios de elegibilidad, se seleccionaron 27 artículos para fundamentar la construcción del protocolo. En la segunda fase, el protocolo fue evaluado por 11 especialistas con experiencia en nutrición clínica, oncohematología, oncología y/o terapia nutricional enteral, mediante un cuestionario estructurado con escala tipo Likert. El análisis de la concordancia entre los jueces se realizó a través del Índice de Validez de Contenido (IVC), considerando 0,80 como valor mínimo aceptable. **Resultados:** El protocolo obtuvo un IVC global de 0,87, lo que indica buena validez de contenido. **Conclusión:** El protocolo presenta contenido validado por especialistas, representando una herramienta potencial para la práctica clínica. No obstante, se destaca la necesidad de validación con los usuarios finales para confirmar su aplicabilidad.

Palabras clave: Protocolos Clínicos/normas; Nutrición Enteral/normas; Trasplante de Células Madre Hematopoyéticas; Neoplasias Hematológicas/dietoterapia.

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is one of the established treatments for various benign and malignant hematological diseases, contributing to their remission[1]. Allo-HSCT consists of administering a chemotherapy-based conditioning protocol to induce immunosuppression, reducing, or eradicating existing neoplastic cells, and later infusing the patient with hematopoietic stem cells (HST)[2].

During myeloablative conditioning, drug-induced toxicities may occur, causing severe side effects that may reach gastrointestinal tract cells (GIT), generating poor absorption and symptoms like mucositis, dysgeusia, nausea, vomiting, diarrhea, which favors insufficient oral intake[3,4]. Consequences of a reduced caloric intake, added to the catabolic effect of the therapy and its complications, result in intense deterioration of the nutritional state, significantly affecting the clinical outcome and patient quality of life even after late allo-HSCT[1,4].

The lack of proper nutritional support during HSCT may result in quick severe malnutrition, which is considered an independent risk factor for post-HSCT mortality[5]. Upon admission, HSCT patients are already considered at risk of malnutrition from the stage of nutritional screening[6]. Additionally, patients who, due to reduced oral intake, do not meet 60% of their daily energetic needs for a continuous period of three days, but maintain an adequate GIT function, are recommended to undergo enteral nutritional therapy (ENT)[7,8]. Due to gastrointestinal toxicities, the enteral feeding catheter is recommended to be inserted up to D+3[9,10].

Currently, consensus and national and international guidelines, such as the Brazilian Nutritional Consensus in Hematopoietic Stem Cell Transplantation[9], Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN)[11], the American Society for Parenteral and Enteral Nutrition (ASPEN)[12] and the European Society for Parenteral and Enteral Nutrition (ESPEN)[8] recommend enteral nutrition (EN) as a first-line nutritional support for patients submitted to allo-HSCT.

Recent evidence has shown significant clinical benefits of early ENT implementation. The anticipated introduction of EN may contribute to intestinal microbiota diversity, reduced treatment-related mortality, and lower incidence of graft versus host disease (GVHD), especially in more severe cases that involve the intestines[1,13]. Moreover, it has demonstrated shorter hospitalization periods and greater survival at 100 days, when compared to exclusively parenteral nutrition[14].

Although the literature consistently reinforces the importance of EN as a sidekick in the allo-HSCT treatment[1,8,9,11-14], clinical protocols that approach the early implementation of ENT are still scarce. In this context, the present protocol aims to fill this gap, playing a fundamental role in qualifying the nutritional care offered at the unit and serving as a staple for other HSCT specialized centers.

Multidisciplinary and interdisciplinary work makes all the difference in the care of patients submitted to allo-HSCT. The integration of nutritionists, doctors, nurses, and other professionals allows for continuous nutritional state assessment, adaptation of feeding support to clinical conditions, and optimization of therapeutic results[15]. This collaborative approach boosts the effectiveness of early ENT, ensuring safer, more individualized, and patient-centered care.

Considering that patients submitted to allo-HSCT present a high nutritional risk and greater mortality risk, this protocol aims to validate and systematize early ENT, with a multiprofessional and interdisciplinary approach. The proposal was developed within the context of a public university high-complexity hospital located in Fortaleza (Ceará State), which has a leading Bone Marrow Transplant Service in Brazil.

METHOD

Methodological study divided into two phases. The first phase consisted of surveying scientific evidence through an integrative literature review in the PubMed and LILACS databases. To elaborate this protocol, researchers sought scientific papers published from 2014 to 2024. The used descriptors both in Portuguese and English were related to nutritional therapy and HSCT, including the terms: *Terapia Nutricional* (nutrition therapy), *dietoterapia* (diet therapy), *apoio nutricional* (nutritional support), *nutrição enteral* (enteral nutrition), *transplante de células hematopoiéticas* (hematopoietic stem cell transplantation), and *transplante de medula óssea* (bone marrow transplantation). Those terms were combined using Boolean operators OR (for synonyms) and AND (for the two main themes).

Of the 178 articles found initially, the following were excluded: duplicates, studies with children, case studies, incomplete texts, and those that did not directly approach assessment or nutritional therapy in the context of allo-HSCT. By the end of the screening process, 27 articles were considered eligible for review and submitted to critical analysis. The analysis criteria included nutritional and clinical outcomes, as well as their applicability in the institution. A shortage of structured and validated protocols for early ENT in the HSCT context was observed, especially in Brazilian institutions. Later, a meeting with the multiprofessional team was conducted to align the next steps and adapt the protocol to current care practices.

The second phase consisted of internal content validation through the analysis of a committee of specialists/judges. Participants were selected by purposive sampling, in which participants with knowledge of the studied issues were purposefully chosen, in addition to a snowball sampling from the referral of eligible participants by the selected specialists[16].

To compose the specialists committee, the Lattes platform was consulted, and professionals with training and experience compatible with the study's subjects were selected. Inclusion criteria and scoring were based in the adaptation of the content validation module proposed by Fehring[17], requiring a minimum score of 6 points. The assessment considered academic titles, experience time in the field, and scientific production, with points attributed according to the following criteria: doctorate with a thesis on the subject (3.5 points); master degree in clinical, oncological, or ENT nutrition (2.5 points); specialization in the interest subjects (2.0 points); publications on the subject (2.0 points); and minimal experience of five years in hospital nutrition (2.0 points). The maximum possible score was 12 points.

For content validation assessment, a Likert-type scale was used, in which specialists could select one out of four options for each item in the protocol: 1 = Disagree, 2 = Neither agree nor disagree, 3 = Agree, and 4 = Completely agree. To measure the proportion of evaluators in agreement with each aspect of the protocol, a Content Validity Index (CVI) was calculated, following Alexandre and Coluci's methodology[18]. The CVI for each item was obtained using the proposed formula, and the items that presented a CVI lower than 0.80 were considered of unsatisfactory validity, and therefore, revised or excluded. The protocol was considered valid when the agreement level was equal to or higher than 80%.

As the specialists were selected, an invitation letter was sent to them by email. Upon accepting participation, they received an Informed Consent Form (ICF), the specialist identification instrument, the instrument with instructions for evaluating the protocol, and the protocol.

This study has been approved by the Research Ethics Committee, report number 7,232,417 (CAAE (submission for ethical review): 83926124.7.0000.5045), in compliance with Resolution 466/2012[19] of the National Health Council.

RESULTS

NUTRITION PROTOCOL FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION: EARLY ENTERAL NUTRITIONAL THERAPY

A full nutritional assessment (NA) is conducted in all patients submitted to HSCT. NA is the first step of nutritional support and must be guided by objective and subjective methods. Preferably, it should be conducted before the start of conditioning, so it is not influenced by the effects of antineoplastic therapy. NA starts in the outpatient clinic environment, to screen individuals with the key characteristics of the target population (see ahead for inclusion criteria) and finishes at the time of hospitalization for HSCT. Still in the clinical environment, the nutritionist educates the patient on the benefits of using ENT early on. The assessment must contain, at least: nutritional risk screening; nutritional anamnesis, with clinical and dietetic data; physical exam; anthropometry; and biochemical assessment.

All efforts are made to conduct nutritional risk stratification within the first 24 hours after hospital admission, not exceeding 48 hours. The tools used were Nutritional Risk Screening (NRS)[20], followed by a Patient-Generated Subjective Global Assessment (PG-SGA)[21]. This patient profile is already considered at nutritional risk according to the NRS illness severity score (≥3). A PG-SGA ≥2 points results indicate nutritional risk and need for counseling and intervention[11,22].

Through nutritional anamnesis, it is possible to collect dietetic and clinical (date of diagnosis, disease type and stage, performed protocols, and treatment phase) patient data. Inadequate food intake is frequently observed and causes weight loss, which is often severe. Anorexia is an early indicator for malnutrition risk, reduced appetite, and food intake, a risk factor unrelated to the patient's initial weight[11].

Dietary intake assessment is conducted both in the clinic and hospital environments using quali-quantitative methods, through food recall and dietary history. With that in mind, analysis of food history in previous hospitalizations and clinic visits is conducted to track usual behaviors that suggest partial reduction in food intake, enabling the determination of a daily deficit percentage(>25%, >50%, or >75% of energetic needs), and consequently, caloric deficits over time[11].

In hospital admission, the following anthropometric measurements are collected: current weight, height, upper arm circumference (UAC), calf circumference (CC), triceps skinfold (TS), and thickness of the adductor pollicis muscle (TAPM), in addition to information previously collected through PG-SGA, like usual weight (one month and six months ago) and physical exam. Nutritional diagnosis becomes more precise through the following indicators: body mass index (BMI); weight loss percentage (WL%) over the recent months (one, three, or six months); UAC adequacy percentage (UAC% adequacy); CC reduction.

Through this assessment, it is possible to identify those individuals with cancer cachexia, whose identification

criteria include BMI<20 kg/m² with a history of non-intentional weight loss (>2%) and significant weight loss percentage (>5%) over the last six months. Cachexia affects individuals with advanced cancer and is characterized by a multi-factorial syndrome that causes appetite loss, weight loss, and skeletal muscle loss. Consequently, it highly compromises quality of life, reducing functionality, survival, and increasing the treatment's toxicity[23].

It is extremely important to assess the muscle mass of cancer patients, since, in addition to helping identify cachexia and sarcopenia, it is also associated with complications in the antineoplastic treatment, reduction of quality of life, and mortality. Thus, sarcopenia screening is done at the outpatient clinic to identify patients with a higher risk of complications. Strength assessment is done through the "Strength, Assistance for walking, Rise from a chair, Climb stairs and Falls" (SARC-F)[24] questionnaire, which, when combined with CC and hand grip strength (HGS), improves screening sensitivity[11]. HGS must be assessed using a hydraulic dynamometer, measured in both arms three times alternately. The highest reached value is recorded[25]. The diagnostic and screening tests suggested are listed as follows. Hypoalbuminemia (<3.5 mg/dl) must be interpreted as a nutritional state indicator only in the absence of significant inflammation, reflected by a C-reactive protein (CRP) <10 mg/l[26].

- Hemogram (hemoglobin, leukocytes, neutrophils, platelets, etc.)
- Electrolytes (phosphorus, potassium, sodium etc.)
- Plasmatic proteins (albumin, globulin, and plasmatic proteins)
- Kidney function (urea and creatinine)
- Liver function (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase)
- Blood glucose
- Ferritin
- Others

Adult patients (≥18 years) admitted to the bone marrow transplant ward of the Fortaleza (Ceará) university hospital, who would be submitted to myeloablative allo-HSCT and met three or more of the following clinical and nutritional criteria, were included in the protocol[7,11,23].

- B or C score in the PG-SGA
- SARC-F score ≥11
- CC: ≤33 cm (women); ≤34 cm (men)
- HGS: ≤16 kg (women); ≤27 kg (men)
- Albumin ≤3.5 g/dl
- Reduced food intake at home (<75% of the Estimated Energetic Requirement – EER) – period between antineoplastic therapies
- History of low food intake at hospitalization (<60% of the EER) – period between nutritional assessments
- BMI<20 kg/m² with a history of unintentional weight loss (>2%)
- Percentage of significant weight loss (>5%) over the last six months

Patients with a hospitalization period under 72 hours (patients admitted for exams), children, adolescents, and those who refused the indicated therapy were excluded.

Attributions, competencies, and responsibilities of the multidisciplinary team in the care of cancer patients with early ENT were adapted according to Anvisa's RDC Regulation n. 503[27].

NUTRITIONIST

- Assess patients' nutritional state using nutritional subjective and objective indicators based on the protocol
- Elaborate a dietary prescription based on the prescribed feeding route (oral or enteral), following nutritional guidelines
- Select the most appropriate industrialized enteral formula and formulate enteral therapy according to patients' nutritional needs, establishing qualitative composition, fraction, times, and presentation
- Maintain the quality of EN until handover to the professional who will manage the diet
- Adjust dietary prescription following medical consensus, nutritional evolution, and diet tolerance
- Assess diet acceptance and/or tolerance
- Guide patients or caregivers on the procedure
- Promote food and nutritional education

DOCTOR

- Indicate and prescribe the diet route of administration, based on this protocol
- Ensure access and use of the gastrointestinal tract
- Guide patients or caregivers on the procedure
- Assess signs of diet tolerance
- Evolve the diet route of administration, based on this protocol

NURSE

- Proceed or ensure insertion and fixation of the nasogastric tube (NGT)
- Ensure position of the NGT (chest x-ray)
- Ensure maintenance of the route of administration
- Receive EN and ensure its conservation until full administration
- Assess and ensure EN administration following the information contained in the label

- Record administration and tube washing in the dietary prescription and system
- Detect, record, and communicate to the Nutritional Therapy Multiprofessional team and/or the responsible doctor any intercurrence (technical and/or administrative)
- Ensure a clear and precise record of information regarding administration and patient evolution regarding: weight, vital signs, digestive tolerance, and others
- Ensure dressing change and/or fixation of the enteral tube
- Watch over the perfect functioning of infusion pumps
- Ensure that any other drug and/or prescribed nutrients are administered through the same EN route of administration, according to predefined procedures
- Promote health education

NURSING TECHNICIAN

- Help the nurse insert the NGT
- Perform maintenance care to the route of administration (NGT washing, daily switching of equipment, and checking medication administered via NGT)

ENT is characterized by a set of therapeutic procedures that aim to maintain or recover the nutritional state. As recommended by the ASPEN[12] and ESPEN[10] guidelines, which address nutritional support to patients who will undergo HSCT, artificial ENT is a choice for malnourished patients who have reduced food intake or intestinal absorption for prolonged periods[9].

In the context of HSCT, nutritional needs are knowingly heightened, and patients are more prone to gastrointestinal toxicities. Moreover, patients who keep losing weight even three months after allo-HSCT have a higher mortality risk, not attributed to disease recurrence, and worse survival. It is clear that qualified nutritional intervention must be supporting HSCT therapy[9].

The use of ENT with an industrialized, polymeric, hypercaloric, hyperproteic, lactose- and fiber-free formula will be recommended as standard, as it provides a lower risk of contamination, a greater supply of macro and micronutrients, and a lower risk of gastrointestinal intolerances. Intermittent infusion is preferred, with the use of a pump for better control of the infusion flow.

A number 12 enteral tube will be inserted following the institution's Standard Operating Procedure (SOP). The gastric position is preferred for being better tolerated and enabling the use of enteral formulas with a higher osmotic concentration and volume[9]. The EN administration will be done according to the institution's SOP. The following lists some steps that require attention.

- The equipment switch should be done every 24 hours, in the morning period, along with the first diet, following recommendations from the Hospital Infection Control Commission (HICC)
- In the intermittent system, EN should not remain for over four hours at room temperature
- The tube washing must occur immediately before administering the EN with 20 ml of drinking water, and immediately after finishing with at least 40 ml of drinking water
- Proceed to washing the NGT before and after administering medication
- Patients must be instructed to remain seated or with the headrest elevated to 30-45° during EN and at least 30 minutes after administering the diet

Oral diet shall be suspended in the face of clinical conditions such as hemodynamic instability, severe dysphagia or odynophagia, uncontrollable vomiting, intestinal obstruction, grade 4 mucositis, paralytic ileus, bleeding from the gastrointestinal tract, among other complications. The enteral route shall be interrupted in the presence of hemodynamic instability, uncontrollable vomiting, intestinal obstruction, paralytic ileus, bleeding from the gastrointestinal tract, or other clinical complications.

During HSCT, nutritional recommendations include an energetic provision of 30 to 50 kcal per kilogram of body weight a day, with protein amount varying from 1.5 to 2.0 g/kg/day. Glycose ingestion must be limited to 5 g/kg/day. Regarding lipids, it is recommended to avoid the intake of trans fatty acids and to be mindful of the suitability of different types of fatty acids. Saturated fatty acid intake should represent less than 7%-10% of the total energy value (TEV), as per individual cardiovascular risk. Mono-unsaturated fatty acids, however, should correspond to 15% of TEV, while poly-unsaturated fatty acids should compose 5%-10% of TEV. Water recommendation is 1 ml per ingested kcal or 35 ml per kilogram of body weight[9.] Therapeutic change will be indicated based on the evolution of the patient's chosen nutritional route, modification of the diet according to their tolerance, and the need to modulate the diet according to the clinical condition presented.

The nutritionist conducts weekly nutritional state reassessments and re-screenings. The clinical evolution of the patient occurs daily or at least five times/week. The investigation is done through biochemical tests, physical tests, and gastrointestinal symptoms (vomit, gastric residue, distension, diarrhea, and abdominal pain), which signal intolerance to the oral and/or enteral diet, and 24h food recall that leads to progression or regression of ENT.

The assistant doctor should assess the clinical possibility of hospital discharge. All patients submitted

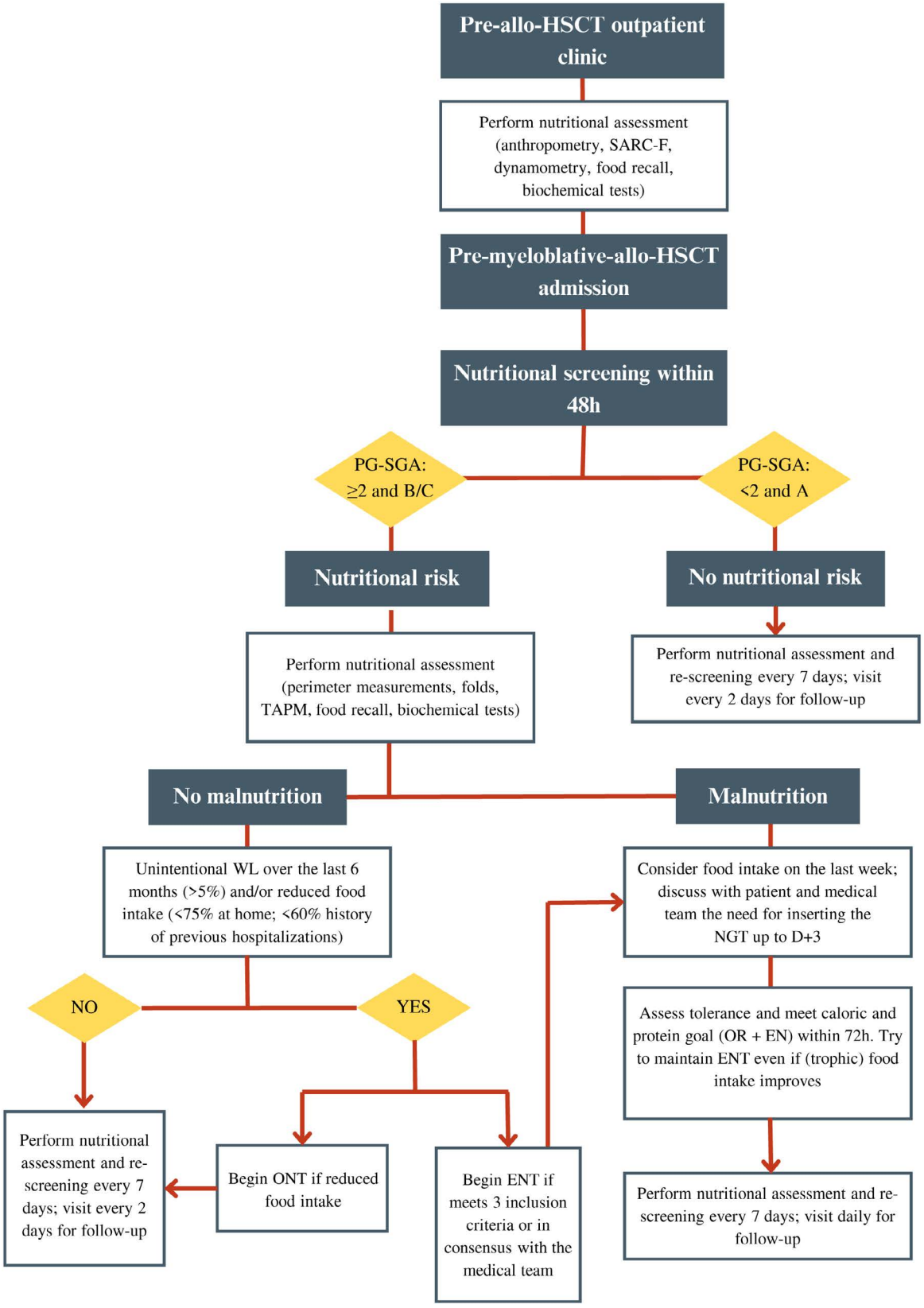

Figure 1. Decision-making flowchart for early enteral nutrition therapy of patients admitted to myeloablative allo-HSCT
Source: Adapted from Barban et al.[9]
Captions: allo-HSCT = allogeneic hematopoietic stem cell transplant; PG-SGA = patient-generated subjective global assessment; TAPM = thickness of the adductor pollicis muscle; SARC-F = Strength, Assistance for walking, Rise from a chair, Climb stairs and Falls; WL = weight loss; ONT = oral nutritional therapy; ENT = enteral nutritional therapy; NGT = nasogastric tube; OR = oral route; EN = enteral nutrition.

Chart 1. Access route selection

Access route	Indication
Oral nutritional therapy	• Diet acceptance or tolerance <70% of EER over the last 3 days
Enteral nutritional therapy	• Oral tolerance <60% of EER over the last 3 days • Severe dysphagia or odynophagia that impairs the oral route diet • Lower consciousness level • Patients who meet the inclusion criteria (see previously listed topic) • Insert the tube preferably until D+1 (in case it does not happen, D+3 is the limit)
Parenteral nutritional therapy	• Unable to use the GIT • Persistent discomfort when using the GIT (distension, worsening diarrhea, fullness, intestinal bleeding, and severe mucositis), with no prospect of improvement • PNT may be associated with ENT and the oral route

Source: Adapted from SBNO[7] and Barban et al.[9]

Captions: EER = estimated energetic requirement; GIT = gastrointestinal tract; ENT = enteral nutritional therapy; PNT = parenteral nutritional therapy.

to HSCT for the first time should receive guidance on nutritional discharge. This guidance should be delivered by a nutritionist and must contain educational material specifically developed for HSCT. In some cases, the nutritionist must assess the need to deliver a quantitative food plan, a nutritional report with an indication for oral supplementation, and/or referral to the outpatient clinic.

VALIDATION BY SPECIALISTS

Among the 19 specialists invited to contribute to the protocol validation, 4 did not respond to the invitation letter, and 15 agreed to participate; however, 4 did not return the completed instrument. In the end, the sample was composed of 11 nutrition specialists (Table 1).

Among the specialists who responded to the protocol evaluation, most were female (91%), had a high professional qualification (54.5% had doctorates), vast experience in hospital/outpatient clinic nutrition (54.5% had over 10 years of experience in the field) and almost all of them had publications in the onco-hematology, oncology and/or ENT subjects (90.9%). Other detailed data can be directly consulted in Table 1.

The classification data of the specialists in the study, according to scoring criteria adapted from Ferhing[17], are listed as follows (Table 2). Demonstrating that there was a predominance of those who met a maximum score of 12 points (36.3%), with an average score of 9.4 points. Thus, the sample was deemed qualified, combining professional experience and academic and research commitment.

As to the process of judging the protocol validation instrument items, the specialists were told to evaluate clarity, concision, diagram representation, understandable language, materials, and methods used, applicability in adult patients, and nutritional recommendations to patients submitted to allo-HSCT. All the items (100%) obtained an agreement level within the predefined (CVI ≥80%), with CVI varying between 0.82 and 1.00. The agreement level with the protocol was 87% (mean CVI: 0.87). This result strengthens confidence in the content and construct validity of the developed protocol.

During analysis, the specialists were instructed to annotate any necessary corrections and suggestions. From these instructions, they suggested relevant propositions that were reviewed and accepted to improve the protocol. For the protocol items that required changes, Chart 2 was elaborated to summarize the topics evaluated by the specialists. During protocol evaluation, some doubts raised by the evaluators were considered, and so, changes were made to the document to better clarify the topics in question.

DISCUSSION

The protocol validation relied on the participation of highly qualified specialists, most with a doctorate and broad experience in hospital clinic nutrition, which reinforces the process's credibility. The suggestions received highlight the importance of interdisciplinary work, enabling protocol adjustments that reflect the daily practice of multiprofessional teams and promote better safety and effectiveness in the administration of early ENT. This dialogue between scientific evidence and clinical experience reinforces the protocol's responsiveness to the actual context of application.

Furthermore, the implementation of early ENT in patients undergoing allo-HSCT has been associated with positive clinical outcomes, including decreased mortality, improved survival, lower incidence of GVHD, maintenance of intestinal microbiota, reduced hospitalization time, and lower incidence of infections[1,13,14]. Given that, the

Table 1. Distribution of specialists according to sex, age group, time since graduation, professional occupation, time working in hospital/outpatient clinical nutrition, professional qualification, and journal publication. Fortaleza, Ceará (2024)

Variables	n	%
Sex		
Female	10	91
Male	1	9
Age group (Years)		
<40	8	72.7
40-60	2	18.2
>60	1	9.1
Time since graduation in nutrition (years)		
<10	2	18.2
10-20	7	63.6
>20	2	18.2
Professional occupation		
Hospital clinic	5	45.4
Hospital clinic/Teaching	1	9.1
Outpatient clinic	2	18.2
Clinical nutrition management/ coordination	2	18.2
Teaching	1	9.1
Time working at hospital/outpatient clinical nutrition (years)		
<10	5	45.5
10-20	5	45.5
>20	1	9
Professional qualification (highest title)		
Doctorate	6	54.5
Master's degree	4	36.4
Specialization	1	9.1
Journal publication (onco-hematology, oncology, and/or enteral nutritional therapy)		
Yes	10	90.9
No	1	9.1

Table 2. Score used to distribute specialists. Fortaleza, Ceará (2024)

Score	n	%
12	4	36.3
10	2	18.2
8.5	1	9.1
8	1	9.1
6.5	2	18.2
6.0	1	9.1

Source: Adapted from Ferhing[17].

protocol not only standardizes nutritional care but also offers practical support to the team, promoting continuous improvement in patient care and quality of life.

Sarcopenia, initially associated with aging alone, is now acknowledged as a process that can start before old age, with multiple causes in addition to aging. These new perceptions have important implications for preventive and therapeutic strategies, including the elaboration of this protocol[30].

An issue highlighted by two specialists (18.2%) was using the threshold value for HGS in elders. Although the European Working Group on Sarcopenia in Older People (EWGSOP2) is directed towards the elderly population, HGS is an important indicator of sarcopenia in several age groups. Additional studies are needed to validate thresholds for young adults. According to the EWGSOP2 recommendation, values below -2.5 standard deviation from the average local young population are considered, with thresholds of <29.7 kg for men and <16.2 kg for women, according to a study conducted in the Brazilian young adult population[28].

CC measurement is the anthropometric indicator that presents the greatest correlation with muscle mass[24]. In the absence of methods such as electric bioimpedance, imaging methods such as bone densitometry (DXA) or computerized tomography, anthropometry may be applied as it represents a non-invasive, inexpensive, and easy-to-perform alternative in a hospital setting[30].

Although threshold CC values have been originally defined based on studies conducted in elders, a study by Gonzalez et al.[29], which included 17,856 adults (>18 years), showed that, by adjusting thresholds considering variations in body composition related to BMI, sarcopenia assessment is improved. Adjusted CC may be obtained simply by adding 4 cm for individuals with a BMI<18.5, or subtracting 3, 7, or 12 cm for those with a BMI in the 25–29, 30–39, and ≥40 ranges, respectively, in relation to the measurement taken.

One of the specialists suggested adding a nursing attribution of notifying nutrition when the intermittent enteral nutrition goes over its expiry administration deadline, since diet conservation is the nutritionist's responsibility[27]. Intermittent system enteral diets can be kept at room temperature for up to 4 hours after packaging[31]. However, in a hospital setting, it is key to consider manipulation time, transport, and diet administration. Thus, in the university hospital, the protocol defines that diets prepared in the open system should be administered up to 30 minutes after being received from the nursing office. If this deadline is exceeded, the nutrition team must be notified immediately.

Chart 2. Summary of the evaluated items, issues identified, and changes made or suggested by specialists, according to protocol evaluation

Evaluated items	Identified issues	Changes
Nutritional screening	According to NRS (2002), the patient is already considered at nutritional risk, which raises the question of its applicability in this context	Add NRS (2002) score ≥4 to the inclusion criteria
Hand grip strength	Threshold for elders: ≤16 kg (women); ≤27 kg (men)	<16.2 kg (women); <29.7 kg (men)[28]
Calf circumference	Using calf circumference without adjusting for BMI	BMI<18.5 (+4 cm); BMI 25–29 (-3 cm); BMI 30–39 (-7 cm); BMI≥40 (-12 cm)[29]
	Threshold for elders: ≤33 cm (women); ≤34 cm (men)	Adjusting the threshold value to the BMI attenuates the effect of age on calf circumference[29]
Nurse attributions	Not attributing to nurses the task of notifying nutrition on the expiration of the enteral diet	Ensure enteral diet in the intermittent system is administered in the first 30 minutes after receiving it; otherwise, the nutrition team should be contacted
Energetic needs	The recommendation of 30-50 kcal/kg/day is too broad	Malnutrition: 40-50 kcal/kg/day Eutrophy: 35-45 kcal/kg/day Overweight: 35-40 kcal/kg/day Obesity: 30-35 kcal/kg/day
Enteral nutrition	Lack of detailing of enteral nutrition administration: time range and period (day/night)	The standardization of the number of enteral nutrition steps does not apply to the protocol; the steps should be adjusted individually according to the last 24 hours' food recall, as a complement to oral nutrition. The administration period should be during the day, preferably

Source: Bielemann, Gigante, Horta[28]; Gonzalez et al.[29].
Captions: NRS = Nutritional Risk Screening; BMI = body mass index.

Nutritional energy recommendations are defined according to the Brazilian consensus; however, this recommendation is broad and does not consider the individual's nutritional diagnosis[9]. Evaluation and combination of data collected from NA are fundamental for diagnosing malnutrition in oncological patients[32]. Thus, for the nutritional diagnosis of hospitalized patients, it is recommended to consider at least two or more similar indicators, like, for example, BMI-assessed malnutrition and UAC adequacy percentage. From this diagnosis, a consensus was reached among the nutrition team on the distribution of energy ranges.

One of the limitations of this study is the scarcity of recent publications (within the last five years) that address the interface between nutrition and oncology. This limitation restricts the comparison of findings with updated evidence and highlights the need for further studies that address nutritional work in the oncological context, especially in specific populations.

CONCLUSION

The scarcity of structured clinical protocols targeted at early ENT in the context of HSCT reinforces the relevance of the proposal. It must be noted, however, that this manuscript contemplates only the theoretical validation step; for practical application, validation from users will be needed in a later step. The expectation is that, in the future, its implementation will contribute to systematizing interdisciplinary care and optimizing clinical and nutritional outcomes of patients at high nutritional risk, decreasing mortality, and improving clinical results in the post-HSCT.

ACKNOWLEDGMENTS

To the multiprofessional team of the university hospital bone marrow transplant unit, whose collaboration was essential in the methodological step of adapting the

protocol to institutional practices. To the specialists who kindly employed their time, expertise, and critical skills in the assessment and validation of the developed protocol's content. Your contributions were fundamental to ensuring the methodological quality and consistency of this study.

CONTRIBUTIONS

All the authors have substantially contributed to the study design, data acquisition, analysis, interpretation, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the contents associated with the article are included in the manuscript.

FUNDING SOURCES

None.

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Recebido em 8/7/2025
Aprovado em 25/8/2025

Associate editor: Livia Costa de Oliveira. Orcid iD: https://orcid.org/0000-0002-5052-1846
Scientific-editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777