Original Article

Applicability of vector analysis of electrical bioimpedance in the context of hematopoietic stem cell transplantation

Aplicabilidade da análise vetorial da bioimpedância elétrica no contexto do transplante de células-tronco hematopoiéticas

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ABSTRACT

Introduction: Hematopoietic stem cell transplantation (HSCT) carries a high risk of malnutrition and clinical complications. Tools such as the Patient-Generated Subjective Global Assessment (PG-SGA), the Nutritional Risk Index (NRI), and bioelectrical impedance vector analysis (BIVA) have been used to diagnose malnutrition and relate it to clinical outcomes, with BIVA emerging as an alternative to traditional BIA, although it remains scarcely studied in HSCT patients. **Methods:** This retrospective cohort study included 32 patients who underwent allogeneic HSCT at the Hospital Sírio-Libanês, São Paulo, Brazil, between April 2020 and April 2024, all of whom underwent BIA at least once from pre-transplant to the 30th day post-transplant. Statistical analyses included normality tests, Fisher's test, Kaplan-Meier, Log-rank, T-test, and Mann-Whitney, considering a significance level of 5%. **Results:** As a result, 67% of patients assessed by BIVA and NRI and 50% by PG-SGA were classified as not malnourished, but no statistically significant association was observed between nutritional status and the evaluated clinical outcomes. **Conclusion:** While BIVA appears promising due to its ease of graphical interpretation, further studies with larger sample sizes are needed to validate its usefulness and clinical impact in the context of HSCT.

RESUMO

Introdução: O transplante de células-tronco hematopoiéticas (TCTH) implica alto risco de desnutrição e complicações clínicas. Ferramentas como a Avaliação Subjetiva Global (ASG-PPP), o Nutritional Risk Index (NRI) e a análise vetorial da bioimpedância elétrica (BIVA) têm sido utilizadas para diagnosticar desnutrição e associá-la a desfechos clínicos. A BIVA surge como uma alternativa à BIA tradicional, embora ainda pouco estudada em pacientes de TCTH. **Método:** Este estudo de coorte retrospectivo incluiu 32 pacientes submetidos ao TCTH alogênico no Hospital Sírio-Libanês, São Paulo, Brasil, entre abril de 2020 e abril de 2024, que realizaram BIA pelo menos uma vez do pré-transplante ao 30° dia pós-TCTH. As análises estatísticas abrangeram testes de normalidade, Fisher, Kaplan-Meier, Log-rank, Teste T e Mann-Whitney, considerando significância de 5%. **Resultados:** Como resultado, 67% dos pacientes avaliados pela BIVA e NRI e 50% pela ASG-PPP foram classificados como não desnutridos, mas não foi observada associação estatisticamente significativa entre o estado nutricional e os desfechos clínicos avaliados. **Conclusão:** Embora a BIVA se mostre promissora pela facilidade de interpretação gráfica, ainda são necessários estudos com maior amostra para validar sua utilidade e impacto clínico no contexto do TCTH.

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a complex treatment for various hematological and immunological diseases, and its use has increased significantly in recent decades due to greater donor availability and advances in conditioning regimens[1,2]. In 2023, approximately 4,262 procedures were performed in Brazil[3]. During the process, complications such as reduced food intake, increased nutritional demands, gastrointestinal changes, and fluid imbalances can negatively affect patients' nutritional status, especially depending on the intensity of conditioning and the occurrence of graft-versus-host disease (GVHD)[1].

Given the high risk of malnutrition in patients undergoing HSCT, especially after myeloablative regimens[4], it is essential to assess nutritional status prior to transplantation and to monitor it regularly throughout treatment, considering food intake, functionality, anthropometry, and body composition. In this context, the Patient-Generated Subjective Global Assessment (PG-SGA) is an effective tool for identifying cancer patients who may benefit from early nutritional intervention[1]. The Nutritional Risk Index (NRI) has also shown good performance in assessing overall survival and non-relapse mortality in patients undergoing HSCT[5,6].

Among the methods for assessing body composition, bioelectrical impedance analysis (BIA) is characterized as a non-invasive exam widely used as a screening method for sarcopenia and as a possible prognostic predictor in cancer patients[7]. The operating principle of BIA is based on the passage of an electric current through the body, resulting in resistance (R) and reactance (Xc) data[8]. It is understood that body tissues offer different opposition to the passage of electric current, since higher concentrations of water allow greater current flow. Therefore, patients in a hyperhydrated condition may show overestimated lean mass values, which can impair the interpretation of their body composition using this method[9].

To address BIA's limitation, R and Xc data can be used for more comprehensive evaluations of body composition through bioelectrical impedance vector analysis (BIVA). This approach allows for detailed interpretations not only of tissue hydration changes but also for evaluating patients' lean mass, providing a more complete view of nutritional and body status[10]. Preliminary studies have suggested the use of BIVA as a complementary method for diagnosing malnutrition in hemodialysis patients[11], a population that shares significant similarities with those undergoing HSCT, especially regarding the risk of malnutrition and fluid imbalance.

In the oncology setting, previous research has indicated that BIVA can be a valuable tool for monitoring changes in body composition in individuals with non-metastatic breast cancer[12]. Additionally, recent studies have shown that this tool was also able to identify significant changes in body composition in patients with gastrointestinal cancer[13]. It is widely discussed that there is considerable potential for improving this tool, and further investigations are needed so that BIVA can effectively assist healthcare professionals in personalizing therapy for cancer patients according to their physiological specificities[10].

Despite advances in the application of BIVA in cancer patients, studies dedicated to the population undergoing HSCT are still lacking. Given the relevance of assessing body composition in this group and the possibility of using an innovative and easily applicable tool, this study is based on the hypothesis that BIVA may be useful for early identification of malnutrition after transplantation.

The justification for this research is based on the lack of studies focused on the use of BIVA in transplant recipients, especially since, although PG-SGA and NRI are already employed, both present limitations when applied to this population. The NRI has shown potential in recent research, while there is little data on the effectiveness of the PG-SGA in this scenario. Therefore, comparing BIVA with these tools may significantly contribute to improving nutritional diagnosis and clinical follow-up.

The main objective is to investigate the ability of BIVA to detect malnutrition in patients who have undergone HSCT, comparing its performance to the results of the NRI and the PG-SGA. Secondarily, the study aims to evaluate how the diagnoses from these tools relate to important clinical outcomes, such as overall survival, non-relapse mortality, occurrence of GVHD, and times to neutrophil and platelet engraftment. It also plans to describe the distribution of patients in the different quadrants of the bioimpedance vector graph, monitoring nutritional status from pre-transplant to the thirtieth day after the procedure (D+30).

METHODS

This retrospective cohort study was conducted by analyzing data obtained from electronic medical records of a private tertiary hospital. The project was approved by the Research Ethics Committee under No. 7,176,824, on October 22, 2024. The requirement for informed consent was waived due to the retrospective nature of the study and the use of secondary data routinely collected in medical records. All data were used exclusively for this research, confidentiality was guaranteed, and the researcher signed

a confidentiality agreement to ensure the privacy of participants, in accordance with Resolution 466/12 of the National Health Council.

The analyzed population comprised patients of both sexes who underwent allogeneic HSCT, whether related or unrelated, as part of the treatment for malignant hematological diseases, between April 2020 and April 2024. Individuals who underwent a bioelectrical impedance analysis in at least one nutritional assessment between the pre-transplant period and the thirtieth day after the procedure (D+30) were included. Patients under 19 years of age were excluded. The sample was defined by convenience, according to the availability of electronic records and institutional databases.

Nutritional data from patients undergoing HSCT were collected in the pre-transplant, D0, D+15, and D+30 phases, as per institutional protocol, to monitor changes in nutritional status. The collected information included weight, height, sex, age, oncological diagnosis, source of stem cells, HCT-CI score, and conditioning regimen. For analysis of the distribution of patients on the RXc tolerance ellipses, impedance (Z) and Xc data obtained by bioimpedance (InBody S10) at 50 Hz were used. R values were calculated and entered into the BIVA Software 2002[14], according to established methodology.

For the RXc graph, references relative to the adult Italian population were used. Patients plotted outside the 75% tolerance ellipse in the lower and upper right quadrants, corresponding to cachexia and thinness according to the software guide, were considered "malnourished" in this study[15]. The remaining patients were classified as "not malnourished."

Data from previous applications of the PG-SGA were collected from electronic medical records, as this tool is used as a standard for nutritional assessment in the outpatient setting of the institution. NRI was applied retrospectively based on medical record data. This analysis was conducted exclusively in the pre-transplant phase, aiming to assess the ability to detect malnutrition before HSCT, a crucial step for patient prognosis. For the application of the NRI, data on patient weight loss available in the records, along with serum albumin values, were collected.

To make the data from this study comparable among the different tools, a standardization of nutritional classifications was adopted. Thus, patients considered "A = well-nourished" by the PG-SGA and those with a score ">100" on the NRI were grouped as "not malnourished." On the other hand, those assessed as "B = moderately malnourished or at risk of malnutrition" or "C = severely malnourished" by the PG-SGA, as well as those with scores of "97.5 to 100 = mild malnutrition," "83.5 to 97.5 = moderate malnutrition," and "<83.5 = severe malnutrition" by the NRI, were all classified simply as "malnourished" in this study[16,17].

To investigate the association between diagnoses made by BIVA, PG-SGA, and NRI with clinical outcomes within one year after HSCT, records of overall survival, non-relapse mortality, occurrence of GVHD, and engraftment times were accessed from medical records. Additionally, data on phase angle (PA), skeletal muscle mass index (SMI), and extracellular water ratio (ECW) obtained by bioimpedance were analyzed to enrich the BIVA assessment of cellularity, muscle mass, and patients' fluid balance.

The adequacy of nutritional status according to SMI values followed the cut-off points defined by the equipment used: values above 7 kg/m^2 for men and 5.7 kg/m^2 for women were considered adequate[18]. For phase angle, the classification proposed by Gupta et al.[19] was adopted, which considers values below 5 as inadequate, as they are associated with worse prognosis, and values above as appropriate. The ECW assessment used the ideal range stipulated by the bioimpedance equipment, between 0.360 and 0.390. Results above this range were classified as insufficient[20].

Descriptive analysis of qualitative variables used simple and percentage distribution tables; quantitative variables were described by mean and standard deviation, with normality assessed by the Shapiro-Wilk test. Associations between BIVA, PG-SGA, NRI diagnoses, and clinical outcomes were analyzed bivariately. For the qualitative variable GVHD outcome, Fisher's exact test was applied; for overall survival and non-relapse mortality at one year, Kaplan-Meier curves and the Log-rank test were used; and for engraftment times, the unpaired Student's t-test or Mann-Whitney test was used. The significance level was set at 5% ($p \leq 0.05$), and analyses were performed in SPSS v22.0. The distribution of patients in the quadrants of the bioimpedance graph was presented graphically, without statistical testing.

RESULTS

Data from 32 patients who underwent allogeneic hematopoietic stem cell transplantation were analyzed, with a mean age of 54.5±16.3 years and a predominance of females (54.9%). The main diagnosis recorded was acute myeloid leukemia, accounting for 38% of the cases. Regarding clinical risk, 28% of patients had an HCT-CI score equal to or greater than 4, indicating a higher probability of non-relapse mortality and complications. As for the type of transplant, there was a predominance of haploidentical donors (62%) and peripheral stem cell sources (84%). The most commonly used conditioning regimen was based on

fludarabine and busulfan (44%), with reduced intensity conditioning adopted in 75% of cases (Table 1).

The analysis of medical records showed that 30 patients underwent a complete nutritional assessment prior to transplantation, while two cases lacked sufficient data for the application of BIVA and PG-SGA. There was also a notable absence of albumin values in the pre-transplant period, making it impossible to use the NRI for part of the sample and resulting in the inclusion of only 21 patients in this specific analysis.

In the pre-transplant period, the mean body mass index was 25.3±3.5 kg/m^2, with a predominance of eutrophic patients (67%). According to BIVA, 67% were classified as not malnourished; the assessment by PG-SGA identified half of the patients in this condition, while the NRI also indicated that 67% were not malnourished (Table 2). The analysis of SMI showed adequacy in 90% of the cases. Regarding the phase angle, only 40% had values considered adequate. The evaluation of the extracellular water proportion indicated that 47% of patients had results below the reference range (Table 2).

The analysis of the associations between the methods BIVA, SGA-PPP, and NRI and the clinical outcomes of overall survival, non-relapse mortality at one-year post-HSCT, and occurrence of GVHD did not identify statistically significant results capable of establishing the impact of nutritional status as assessed by these tools (Table 3; Figures 1-3). Nevertheless, it was observed that, regardless of the instrument used, nutritional status was relevant to the outcomes analyzed.

Table 1 – Clinical characteristics of patients undergoing allogeneic HSCT.

	Total
Number of patients	32
Age in years, mean (range)	54 (20-74)
Male sex, n (%)	13 (41)
Oncological diagnosis, n (%)	
Hodgkin lymphoma	1 (3)
Non-Hodgkin lymphoma	1 (3)
Acute lymphoblastic leukemia	10 (31)
Acute myeloid leukemia	12 (38)
Chronic myeloid leukemia	1 (3)
Multiple myeloma	1 (3)
Myelofibrosis/myeloproliferative syndrome	2 (6)
Myelodysplastic syndrome	4 (13)
HCT-CI Score, n (%)	
<3	23 (72)
≥3	9 (28)
Donor, n (%)	
Haploidentical	20 (62)
Related	5 (16)
Unrelated	7 (22)
Source of cells, n (%)	
Bone marrow	5 (16)
Peripheral blood	27 (84)
Conditioning, n (%)	
RIC	24 (75)
MAC	8 (25)
Conditioning, n (%)	
Fludarabine	2 (6)
Fludarabine and Cyclophosphamide	13 (41)
Fludarabine and Busulfan	14 (44)
Fludarabine and Melphalan	1 (3)
Cyclophosphamide	2 (6)

n = sample size; HCT-CI score = hematopoietic cell transplantation–specific comorbidity index; RIC = reduced intensity conditioning; MAC = myeloablative conditioning.

Table 2 – Nutritional status in the pre-transplant stage of patients undergoing allogeneic HSCT.

	Total
BMI classification, n (%)	
Underweight	1 (3)
Normal weight	20 (67)
Overweight	7 (23)
Obesity	2 (7)
BIVA classification, n (%)	
Not malnourished	20 (67)
Malnourished	10 (33)
PG-SGA classification, n (%)	
Not malnourished	15 (50)
Malnourished	15 (50)
NRI classification, n (%)	
Not malnourished	14 (67)
Malnourished	7 (33)
SMI adequacy, n (%)	
Adequate	27 (90)
Inadequate	3 (10)
PA adequacy, n (%)	
Adequate	12 (40)
Inadequate	18 (60)
ECW adequacy, n (%)	
Adequate	16 (53)
Inadequate	14 (47)

n = sample size; BMI = body mass index; BIVA = bioelectrical impedance vector analysis; PG-SGA = patient-generated subjective global assessment; NRI = nutritional risk index; SMI = skeletal muscle index; PA = phase angle; ECW = extracellular water.

Table 3 – Analysis of the impact of nutritional status assessed by BIVA, SGA-PPP, and NRI on the outcomes of overall survival, non-relapse mortality at one year post-HSCT, occurrence of GVHD, and average time to neutrophil and platelet engraftment.

	N	OS (%)	TRM (%)	GVHD (%)	NE time (days)	PE time (days)
BIVA						
Not malnourished	20	65	25	85	20	33
Malnourished	10	70	30	80	18	24
p-value	1	1	1	1	0,627	0,887
SGA-PPP						
Not malnourished	15	73	20	87	20	24
Malnourished	15	60	33	80	19	52
p-value		0,7	0,682	1	0,561	0,647
NRI						
Not malnourished	14	71	21	93	18	29
Malnourished	7	57	43	57	19	31
p-value		0,638	0,354	0,088	0,387	0,130

n = sample size; BIVA = bioelectrical impedance vector analysis; SGA-PPP = patient-generated subjective global assessment; NRI = nutritional risk index; OS = overall survival; TRM = transplant-related mortality; GVHD = graft-versus-host disease; NE time = neutrophil engraftment time; PE Time = platelet engraftment time.

Patients considered not malnourished according to SGA-PPP and NRI assessments showed better overall survival rates, 73% and 71% respectively.

On the other hand, the BIVA assessment showed a different pattern: patients classified as not malnourished showed a trend toward lower survival (65%) compared to malnourished patients (70%). Regarding non-relapse mortality, all tools indicated a higher incidence among malnourished individuals. As for GVHD, the highest frequency was observed among those not malnourished, regardless of the assessment method. In total, 27 patients (84%) developed some form of GVHD, with the acute manifestation being predominant (81%), while the chronic form was recorded in 34% of cases. In both the acute and chronic presentations, non-malnourished patients, according to any of the tools, had a higher prevalence.

There was no significant association between the nutritional classification of patients by the analyzed tools and neutrophil and platelet engraftment times (Table 3). The graphical analyses show the survival curves for each method evaluated: Figure 1 presents data related to BIVA (p=0.679), Figure 2 corresponds to SGA-PPP (p=0.462), and Figure 3 refers to NRI (p=0.679).

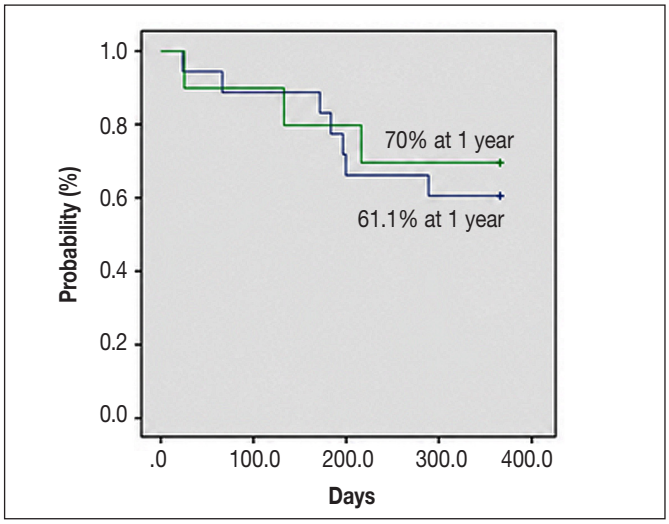

Figure 1 - *Cumulative one-year survival after HSCT according to patient classification by BIVA. Not malnourished: 61.1% vs. Malnourished: 70% (p=0.679).*

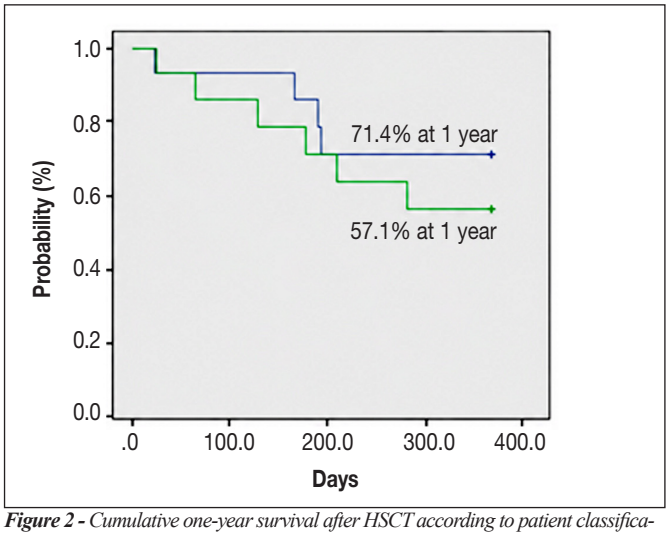

Figure 2 - *Cumulative one-year survival after HSCT according to patient classification by SGA-PPP. Not malnourished: 71.4% vs. Malnourished: 57.1% (p=0.462).*

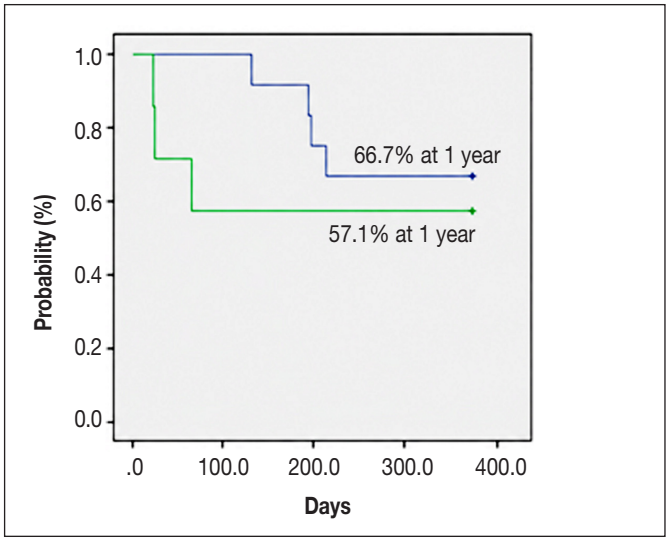

Figure 3 - *Cumulative one-year survival after HSCT according to patient classification by NRI. Not malnourished: 66.7% vs. Malnourished: 57.1% (p=0.679).*

Figure 4 shows the distribution of the study patients within the quadrants of the bioimpedance vector graph at the pre-HSCT, D0, D+15, and D+30 phases. It should be noted that, due to the absence of complete data in the institutional records, a homogeneous evaluation at all stages was not feasible. Thirty patients were analysed at the pre-transplant and D0 phases, 28 at D+15, and 25 at D+30.

In the pre-HSCT phase (Figure 4A), 33% of patients were positioned outside the 75% tolerance ellipse, distributed in the lower and upper right quadrants and classified as malnourished according to the methodology used. At the time of infusion of the haematopoietic stem cells, on D0 (Figure 4B), the prevalence of malnutrition increased to 50%. Fifteen days after the procedure (D+15), this percentage rose to 57% (Figure 4C), remaining similar at 56% on D+30 (Figure 4D).

It is important to highlight that, regarding the patients' location on the graph, those positioned at the top indicate dehydration; those on the left correspond to obesity or hypertrophy; those on the right suggest malnutrition or sarcopenia; and those in the lower region present with oedema.

DISCUSSION

The study assessed the effectiveness of BIVA in diagnosing malnutrition in patients undergoing HSCT, comparing it with other methods and relating the diagnoses to key clinical outcomes. Limitations included the small number of participants and data heterogeneity, which hindered robust statistical analyses and prevented definitive conclusions. Notably, there was an absence of albumin values at the pre-transplant stage. This is an important factor, as according to the literature, patients with albumin below 3.2 g/dl have significantly lower disease-free survival[1], which may impact clinical planning and underscores the need to improve data collection within the service.

However, as described in the results, the nutritional status of patients in the pre-transplant period appears to be a relevant factor for their prognosis. Patients assessed as not malnourished by the SGA-PPP and NRI tools showed better overall survival rates compared to those classified as malnourished. These findings are consistent with scientific literature, which indicates that patients undergoing HSCT and classified as malnourished by SGA-PPP have higher

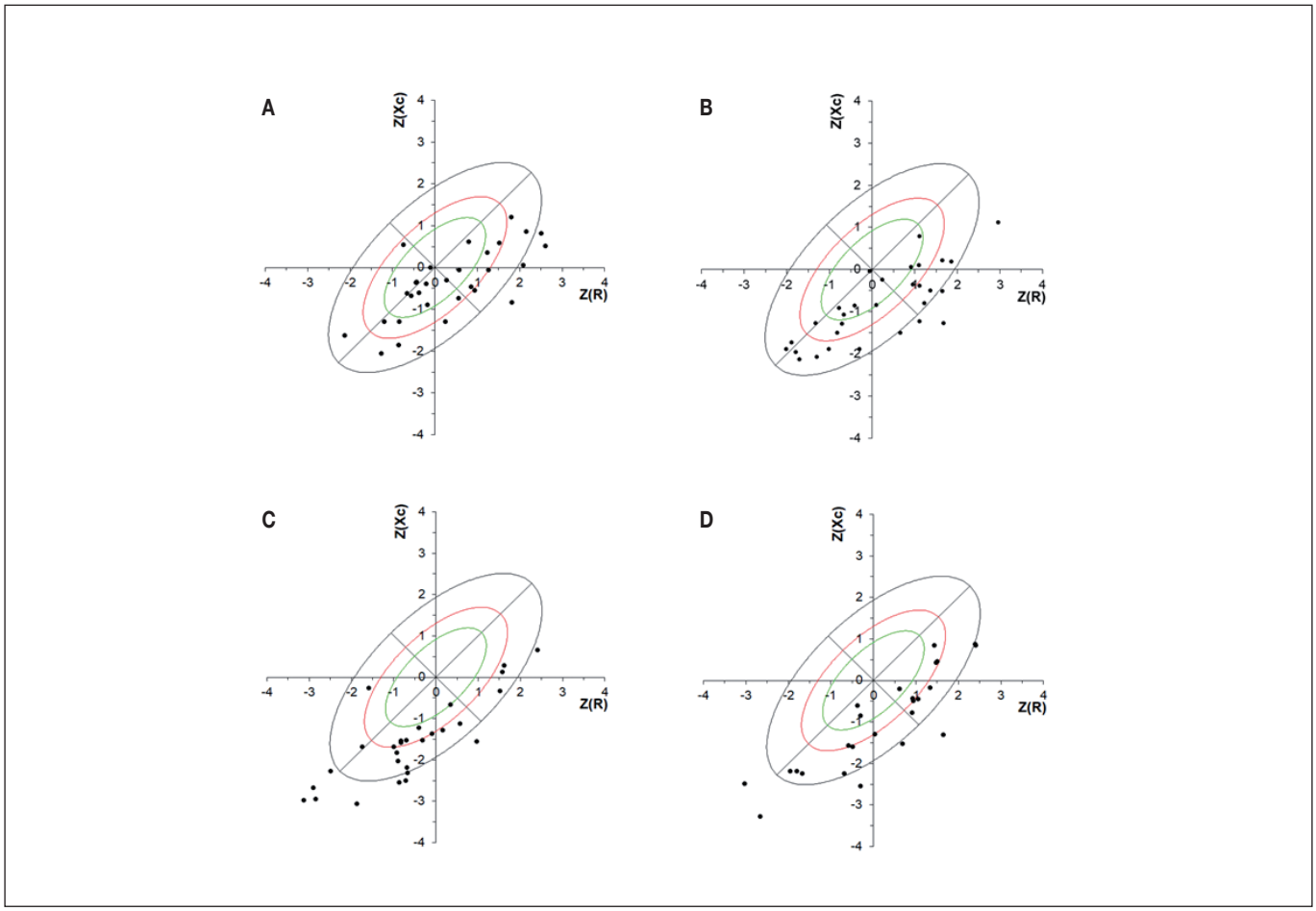

Figure 4 - *Distribution of patients undergoing HSCT across the quadrants of the bioimpedance vector graph. A = pre-HSCT phase. B = D0. C = D+15. D = D+30.*

mortality and a negative impact on survival, highlighting the importance of accurate nutritional diagnoses in this context[21]. Similar results were observed with the use of NRI, in which lower index values were associated with lower overall survival and a higher incidence of non-relapse mortality, as shown in a previous retrospective cohort study[6].

On the other hand, BIVA revealed results different from the other variables analysed, suggesting that patients classified as malnourished tended to have higher survival, although without statistical significance. There is still no consensus in the literature regarding the use of BIVA to explain this divergence in relation to other nutritional assessment tools. One possible explanation is that malnourished patients, being at greater risk of comorbidities and organ dysfunction according to the HCT-CI, may have been subjected to lower-intensity conditioning protocols, which are associated with lower non-relapse mortality. It is worth noting that, unlike traditional methods, BIVA uses objective parameters obtained through body composition examination, without considering subjective aspects of nutritional status, which may influence the results. Furthermore, the absence of statistical significance and the small sample size limit the robustness and interpretation of the findings.

Regarding GVHD, a higher incidence was identified in patients considered not malnourished by the three tools evaluated. These findings partially align with the literature, which points to obesity as a factor that can negatively influence HSCT outcomes, especially in allogeneic transplants, with this connection being less evident in autologous procedures[22]. Additionally, other studies suggest that a high body mass index is associated with higher rates of acute GVHD, infections, and mortality, reinforcing the role of obesity as a risk factor[23]. However, the topic remains controversial, as there is evidence indicating that malnutrition may be an even more relevant element, especially for the chronic form of GVHD[1]. Moreover, previous research using NRI in individuals undergoing HSCT found that higher index values (indicative of not malnourished patients in this study) were also associated with higher incidence of acute and chronic GVHD, corroborating the data presented here[6]. These results reinforce the need for further investigations to more precisely elucidate the influence of nutritional status on the occurrence of GVHD.

Sugizaki et al.[11] demonstrated in a recent study that BIVA, when combined with the 7-point PG-SGA, contributes to a more accurate analysis of malnutrition in patients on haemodialysis, by providing information on cellularity and hydration. Similarly, the findings of this study support the potential of BIVA as a complementary tool in the nutritional assessment of patients undergoing HSCT. The graphs in Figure 4 clearly illustrate the reduction in mass and increase in fluids throughout the transplant, showing a pattern of patient displacement in the ellipses, especially in critical periods such as conditioning and marrow aplasia, as shown in images B, C and D. Additionally, a higher concentration of points is observed in the lower region of the graph, indicating an increase in fluids, a frequent phenomenon during HSCT. This change may be attributed to cachexia, a multifactorial syndrome involving significant weight loss, muscle atrophy, and systemic inflammation, which differs from simple malnutrition due to its strong association with exacerbated inflammatory response and metabolic changes that intensify muscle catabolism[24].

In the context of transplantation, patients' nutritional status tends to be compromised due to the conditioning regimen, the period of aplasia, and complications such as infections and toxicities[1]. This highlights the need for effective nutritional strategies, especially to prevent loss of muscle mass. When bioelectrical impedance is used as the main method for assessing body composition, BIVA emerges as a relevant tool to complement the interpretation of results. In this study, it was found that, according to SMI cut-off points, only 10% of patients presented muscle mass inadequacy. However, AEC identified increased fluid in 47% of cases. Such a scenario of hyperhydration may interfere with SMI analysis, reducing its accuracy in assessing these patients.

By using BIVA as a complementary method, it is possible to visually identify increased fluids and the displacement of patients towards areas of muscle mass inadequacy, correcting possible misinterpretations based solely on SMI obtained by BIA. The BIVA Software 2002 enables the creation of individual graphs to monitor the nutritional evolution of patients during HSCT, making the method useful for monitoring body mass and fluids. This study reinforces the importance of BIVA as a complementary tool in clinical practice and highlights the need for multicentre and methodologically robust studies to validate and enhance nutritional monitoring, especially by assessing the impact of early interventions in at-risk or already malnourished patients.

CONCLUSION

BIVA analysis demonstrates potential as a complementary tool to traditional nutritional assessment methods in patients undergoing HSCT, by providing more detailed information on body composition and nutritional status. Its practical applicability and the possibility of integration into longitudinal follow-up add value to clinical routines. However, this study has important limitations, such as the small sample size and the retrospective design conducted in only one center, which restrict the generalizability of the results. Therefore, it

is essential to conduct future studies, preferably multicenter and with more robust methodological designs, to validate the role of BIVA in the assessment of malnutrition in the context of HSCT and to deepen the understanding of its impact on clinical outcomes. Furthermore, there is a need for investigations that explore nutritional interventions in the pre-transplant period, with the aim of improving clinical outcomes and nutritional care for this population.

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