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NUTRITIONAL ASSESSMENT IN PATIENTS UNDERGOING INTENSIVE CHEMOTHERAPY FOR ACUTE MYELOID LEUKEMIA

Scientific disciplinary sector: MED/15 - Blood Diseases

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Abstract

Fit patients (pts) with acute myeloid leukemia (AML) are conventionally administered repeated cycles of intensive chemotherapy (CHT), often followed by allogeneic hematopoietic stem cell transplant. Pts need to be hospitalized in a protected setting, they are often prescribed a neutropenic diet and chemotherapy-induced gastro-intestinal toxicity is common. As a result, nutritional imbalance is frequently observed.

Aim of this study was to systematically assess the nutritional status of pts undergoing treatment for AML and to explore early predictors and associations with known nutritional risk scores and relevant clinical outcomes.

Monitoring included a bioelectrical impedance analysis (BIA) performed by a dietitian to assess fat mass (FM), fat-free mass (FFM), body cell mass (BCM) and the phase angle (PhA) together with standard measures (body weight, BW; body mass index, BMI). Variations in nutritional parameters between admission and day 7 (end of CHT, dif7) or between admission and day 14 (dif14) were calculated and tested for correlation with variations of the same parameter at discharge from the same cycle (dif30) or at discharge after the first consolidation (dif60).

From March 2021 to March 2023, 26 pts with newly diagnosed AML (median age 55y, range 21-74) were monitored during a total of 61 cycles of intensive CHT (35 induction cycles, 26 consolidation cycles). Median Nutritional Risk Score 2002 (NRS) at enrolment was 3 (range 2-6). Median follow up for surviving pts is 300 days.

We observed a significant reduction in FFM and BCM during induction cycles. These trends were observed irrespectively of baseline NRS, disease response, or fever lasting more or less than 7 days. NRS was not significantly associated with any nutritional parameter variation.

For FFM, BCM and PhA (but not BW or BMI), dif7 correlated with dif30 for induction and consolidation CHT. For BCM and PhA, both dif7 and dif14 also correlated with dif60. Variations in BCM (but not in BW) at day 7 correlated with weight loss at discharge after a second CHT cycle.

Reduction in BW, BMI and FM at day 7, and of PhA at day 14 were associated with extended length of stay for consolidation CHT cycles only.

No associations were found between nutritional status at admission or its variation and disease response to therapy.

Preliminary results from this study show that BIA could reveal a nutritional deterioration as early as 7 days from admission, before BW changes become informative, and could trigger earlier and more effective support measures.

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Introduction

Fit patients diagnosed with acute myeloid leukemia (AML) are conventionally administered repeated cycles of intensive chemotherapy (CHT), often followed by allogeneic hematopoietic stem cell transplant.[1] These patients face long hospitalizations in a protected setting, where they are often prescribed a neutropenic diet, which implies a markedly reduced food choice availability. Also, chemotherapy is known to potentially cause a wide range of gastro-intestinal toxicities, including nausea, vomiting, diarrhea, dysgeusia, loss of appetite, mucositis. The management of these issues has improved in the last decades (e.g., drugs exist for the prophylaxis and treatment of nausea), but inadequate nutritional intake is still common during treatment and is associated with weight loss, which may be severe. Weight loss has been associated with reduced overall survival in cancer patients.[2]

Malnutrition and cancer

Nutrition plays a crucial role in the treatment of cancer patients. Good nutrition can help patients maintain their strength and energy and reduce the risk of treatment-related side effects.

Nutritional status is the balance between nutrient intake and nutritional need. When nutritional needs are not satisfied, malnutrition occurs, which is a functional, structural, and developmental alteration associated with morbidity, mortality, and reduction in the quality of life. Cancer patients are at risk of developing protein-energy malnutrition. Because of the disease, necessary treatment and complications, the balance between protein synthesis and degradation is altered, and endogenous substrates are mobilized to support the systemic requirements. As a result, protein synthesis in muscles is reduced, while degradation is increased.

Cancer cachexia is characterized by the depletion of muscle protein, which significantly reduces the quality of life and negatively affects physical function and the ability to tolerate treatment.[3] Research into the body composition of cancer patients shows that the loss of skeletal muscle, with or without fat loss, is the primary element of cancer-related malnutrition that predicts the risk of physical impairment, chemotherapy-related toxicity, and mortality.[4] A generally accepted value for severe depletion of muscle mass is an absolute muscularity below the 5th percentile, which can be determined via bioelectrical impedance as the whole-body fat-free mass (FFM) index without bone (men <14.6 kg/m^2; women <11.4 kg/m^2). Muscle mass below these values is strongly associated with mortality and dose-limiting toxicity during chemotherapy in cancer patients.

Furthermore, patients with cancer frequently experience a systemic inflammation syndrome, which can result from different causes (infection, chemotherapy, cancer itself) and vary in degree. Effects of this syndrome are on all relevant metabolic pathways: protein metabolism (reduction of fat and muscle mass, reduction in albumin and other physiological protein synthesis and increase in the production of acute phase proteins), carbohydrate metabolism (insulin resistance and impaired glucose tolerance) and lipid metabolism.

The goals of nutritional and metabolic therapy must place considerable emphasis on maintenance or gain of muscle mass. Since physical activity and performance status are impaired in many patients with cancer and this is often accompanied by a further loss of muscle mass, combined nutrition and physical therapy are recommended.

Malnutrition and acute myeloid leukemia

Patients with acute myeloid leukemia are among those at higher risk of malnutrition. In fact, the general causes of malnutrition already discussed for a population with cancer are exacerbated in a setting where the disease and its treatment are both particularly aggressive. Nutritional status in patients newly diagnosed with AML is invariably subverted because of both a reduced caloric intake and an increased caloric need secondary to the leukemia. Frequently, malnutrition is already present at the time of diagnosis.

Acute myeloid leukemia has a rapid onset, often complicated by the results of cytopenias (infections, bleeding, fatigue), all leading to increased energy consumption. Treatment consists of intensive chemotherapy, which can lead to severe mucositis and invariably determines prolonged neutropenia.

Mainly because of the high risk of infections, patients need to be hospitalized for 4-5 weeks on average in a protected environment, where even the space for physical activity is usually limited. Also, even though evidence is limited to support this practice, patients are often prescribed a "low microbial" diet (meat and fish are allowed only if fully cooked, cured meat is generally not allowed, as well as smoked meat or fish, unpasteurized milk or dairy products or eggs, fresh fruit or vegetables which cannot be peeled and disinfected).[5–7] The reduced food choice availability adds up to a state of anorexia linked to organic (toxicity) and psychological factors and determines a marked reduction in caloric intake.

Therapies for malnutrition in cancer patients

Artificial nutrition is the application of nutrients through enteral tubes (enteral nutrition) or parenteral infusions (parenteral nutrition). Artificial nutrition is indicated if patients are – or are at risk of being – unable to eat adequately (e.g., no food for more than one week or less than 60% of requirement for more than 1-2 weeks). The route of administration usually depends on the gastrointestinal tract's level of function and integrity.[8] If total energy expenditure is not measured individually, artificial nutrition should generally aim to supply 25-30 kcal/kg/day and at least 1g/kg/day of proteins.

Other therapeutic strategies for malnutrition exist and need to be explored before artificial nutrition becomes necessary. The primary approach should be through nutrition counselling provided by a healthcare professional, intended as a dedicated and repeated process that involves a comprehensive understanding of nutritional concepts, leading to lasting changes in eating habits.

Although the best way to maintain or increase energy and protein intake is through regular food, when this is not possible, oral nutritional supplements (ONS) are recommended in addition to counselling. These are commercially available and nutritionally complete nutrient mixtures that are consumed orally to supplement the volitional food intake.

Physical therapy, which includes resistance and aerobic exercise training, is crucial for promoting anabolism, retaining and utilizing nutrients, and increasing muscle mass and/or strength. Cancer patients are prone to physical deconditioning, which leads to muscle wasting, catabolic signals, and muscle desensitization to anabolic factors, making physical therapy a vital aspect of nutritional therapy.

In severe cases of malnutrition, pharmacologic agents can be used. These agents are intended to stimulate appetite and gut motility, decrease systemic inflammation and catabolic state, increase muscle mass.[8] On the other hand, these agents can have side effects particularly relevant to the onco-hematologic patient (risk of infection associated with corticosteroids; risk of venous thromboembolism associated with progestins), which limit their use in this subset of patients.

Nutritional assessment and screening tools

To assess nutritional status and identify metabolic consequences of malnutrition, patient's nutritional history together with clinical, anthropometric, and biochemical parameters are used.

Nutritional history is collected by the clinician or the trained dietitian and informs on nutritional habits (quality and quantity of usual food intake).

Laboratory exams (dosages of specific proteins with different half-lives in particular) provide information protein balance and nitrogen balance. Useful labs include albumin (half-life: 18-20 days), transferrin (half-life: 8-9d), ferritin, pre-albumin (half-life: 2d), retinol-binding protein (RBP, half-life: 12h).

Anthropometric measures relevant for nutritional assessment include body weight (BW), height (h) and body mass index (BMI = BW/h^2).

Anthropometric measures and laboratory exams may require time to display significant alteration, which may delay a prompt activation of nutritional support measures. Thus, other methodologies are needed for nutritional screening and early detection of patients at risk for malnutrition.

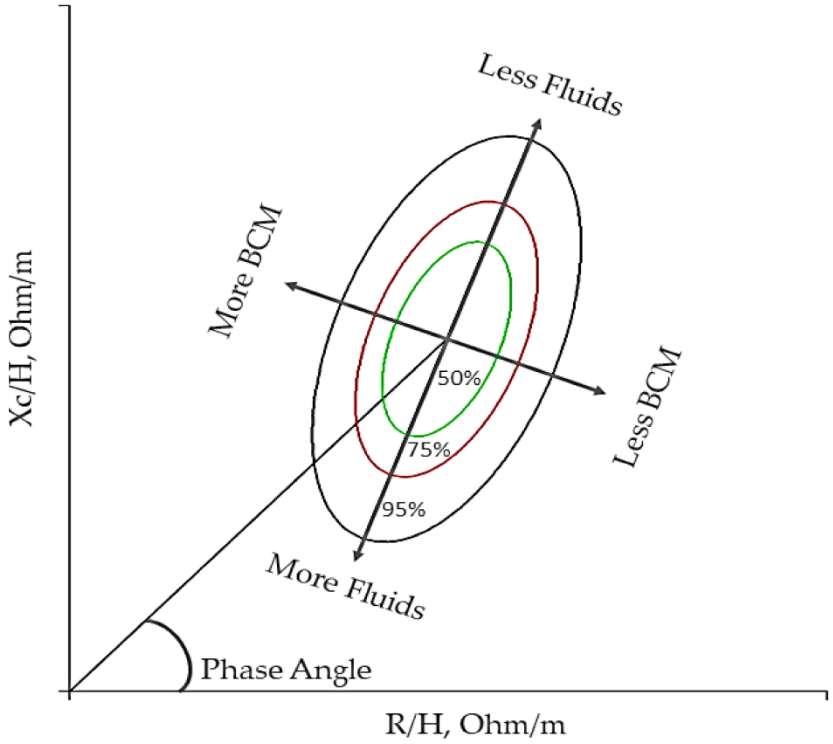

Figure 1. Resistance-reactance nomogram to interpret BIA results.[9]

Bioelectrical impedance analysis (BIA) is a non-invasive, low-cost technique used to estimate body composition in real time. A small, safe electrical current is passed through the body, and the impedance of the tissues to the current is measured in terms of resistance (R) and reactance (Xc).

These values can be normalized for body weight and plotted as a vector (**Figure 1**). Since lean tissue contains more water and conducts the current better than fat tissue, BIA can estimate the amounts of lean body mass (or fat-free mass, FFM) and fat mass (FM), calculate body cell mass (BCM, the metabolically active and functional part of the body), and the phase angle (PhA). In a healthy individual PhA is between 6° and 8°, and the parameter has been associated with prognosis.[10,11] It is a promising screening tool for altered nutritional status and malnutrition.

Nutritional risk scores

Many nutritional risk scores exist and are used in clinical practice.

	Impaired Nutritional Status	Severity of disease (increase in requirements)	
Absent Score 0	Normal nutritional Status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Wt loss >5% in 3 mos or Food intake below 50-75% of normal requirement in preceding week	Mild Score 1	Hip fracture, Chronic patients in particular with acute complications: cirrhosis, COPD, chronic hemodialysis, diabetes, oncology
Moderate Score 2	Wt loss >5% in 2 mos or BMI 18.5-20.5+ impaired general condition or food intake 25-60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery, Stroke, Severe Pneumonia, hematologic malignancy
Severe Score 3	Wt loss >5% in 1 mo or BMI <18.5 +impaired general condition or food intake 0-25% of normal requirement in preceding week	Severe Score 3	Head injury, Bone marrow transplantation, Intensive care patients (APACHE >10)
Score	+	Score	Total Score
Age	If >=70 years old, add 1 to total score = age adjusted total score		
Score >=3: the patient is nutritionally at risk and a nutritional care plan is initiated			
Score <3: weekly re-screening of the patient. If the patient e.g is schedules for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

Figure 2. NRS-2002 scoring system.

MUST (Malnutrition Universal Screening Tool): internationally validated and widely used, consists of three components (BMI, unintentional weight loss, and the presence of acute disease limiting nutrition), which are used to classify patients as low, medium, or high risk for malnutrition.

NRS-2002 (Nutritional Risk Screening): like MUST, evaluates BMI, weight loss and reduced nutrition together with a disease-related cofactor (e.g., +2 points for patients with hematologic malignancy, **Figure 2**). A score equal to or greater than 3 is considered high.[12]

Variables	Undernutrition status			
	Normal	Light	Moderate	Severe
Albumin (g/dL)	≥3.5	3.0–3.49	2.5–2.9	< 2.5
Points	0	2	4	6
Total lymphocyte count (/mm^3)	>1,600	1,200–1,599	800–1,199	<800
Points	0	1	2	3
Total cholesterol (mg/dL)	>180	140–180	100–139	<100
Points	0	1	2	3
Total CONUT score	0–1	2–4	5–8	9–12

Figure 3. CONUT scoring system.

PNI (Prognostic nutritional index): a scoring system based on easily obtainable laboratory results [serum albumin (g/L) + 5 × total lymphocyte count (10^9/L)], independent of classical anthropometric parameters, but potentially unreliable in patients with hematologic malignancies.

CONUT score (CONtrolling NUTritional status): similar to the PNI, this score (**Figure 3**) was more recently developed and also includes total cholesterol.[13]

Aims of the study

Aims of the study were:

1. to systematically analyze the nutritional status of patients undergoing treatment for AML
2. to explore early predictors of malnutrition and their associations with known nutritional risk scores and relevant clinical outcomes.

Patients and methods

The study included patients with newly diagnosed acute myeloid leukemia fit for intensive chemotherapy. Both de novo and secondary AML were included. Patients not treated with chemotherapy or with acute promyelocytic leukemia were excluded.

Nutritional monitoring

Nutritional scores (NRS-2002, PNI, CONUT) were calculated at time of diagnosis. Nutritional screening at time of admission also included body weight, height, BMI, and specific laboratory analyses: total proteins, albumin, prealbumin, ferritin, transferrin, retinol-binding protein.

Patients were admitted to our inpatient setting and nutritional status was prospectively monitored at time of admission, at day 7, at day 14, and at the end of their inpatient stay for either induction chemotherapy or subsequent consolidation cycles.

A bioelectrical impedance analysis was performed weekly by a trained dietitian. Both anthropometric parameters (body weight, BMI) and those measured via BIA (fat mass, fat-free mass, body cell mass and the phase angle) were monitored, and their variation at specific timepoints (dif7 = difference between value at admission and value at day 7; dif14 = difference between value at admission and value at day 14, dif30 = difference between value at admission and value at discharge after induction chemotherapy, dif60 = difference between value at admission and value at discharge after first consolidation chemotherapy) was calculated.

Statistical analysis

Associations of nutritional parameters and their variation at early timepoints with cumulative changes along treatment or with length of stay was tested.

Spearman correlation was used to analyze trends in nutritional parameters with time. T test or Wilcoxon test were used to analyze differences between values at specific timepoints or parameter variations in different groups.

All statistical analysis and graphics were performed with R software, version 4.0.

Results

Between March 2021 and March 2023, 26 patients were enrolled in the study. Patients' characteristics are summarized in **Table 1**.

n	26	
Age (median, range)	55	21-74
Sex	9	34.6%
Female	17	65.4%
Male		
NPM1		
Mut	9	34.6%
Wt	17	65.4%
FLT3		
Mut	6	23%
Wt	20	77%
Cytogenetic risk		23%
Good	3	11.5%
Intermediate	16	61.5%
Poor	7	27%
Allogeneic transplant	6	23%
NRS-2002 score (median, range)	3	2-6
PNI (median, range)	40	29-54

Table 1

Patients were longitudinally followed during treatment and data from a total of 61 cycles of chemotherapy with the distribution as outlined in **Table 2** (fludarabine-based cycles included FLAIE, FLAI, FLAI3, FLAG-Ida; anthracycline-base cycles included 2+5, 3+7, DA, MEC, HAM, CPX-351).

	Fludarabine	Anthracycline	High dose cytarabine	Total
Induction	10	14	0	24
Reinduction	2	9	0	11
Consolidation	1	6	19	26
Total	13	29	19	61

Table 2

Nutritional parameters at admission for each cycle and use of oral nutritional supplements (ONS) or parenteral nutrition (PN) are summarized in **Table 3**. Due to experience in our unit and frequent mucosal damage and thrombocytopenia in patients intensively treated for acute leukemia, enteral nutrition was not used. As expected, all parameters were low at time of admission for consolidation chemotherapy compared with admission for induction chemotherapy, but only different in BCM reached statistical significance.

	INDUCTION (n = 35)		CONSOLIDATION (n = 26)		p
BW (mean (SD))	73.30	(16.90)	70.35	(10.46)	0.436
BMI (mean (SD))	25.26	(3.99)	23.89	(2.57)	0.163
FM (mean (SD))	10.87	(4.96)	10.59	(3.49)	0.819

FFM (mean (SD))	32.65	(4.71)	30.30	(3.61)	0.057
BCM (mean (SD))	15.79	(3.20)	13.92	(2.89)	0.036
PhA (mean (SD))	5.05	(0.88)	4.65	(0.89)	0.117
ONS (n (%))	16	(46)	2	(8)	0.003
PN (n (%))	4	(11)	0	-	0.208

Table 3

Median follow up for surviving patients is 300 days. At time of data cut-off 6 patients had received allogeneic transplant and 5 patients had died. The relatively short follow up does not allow a detailed analysis of potential associations of nutritional parameters with survival.

Nutritional monitoring

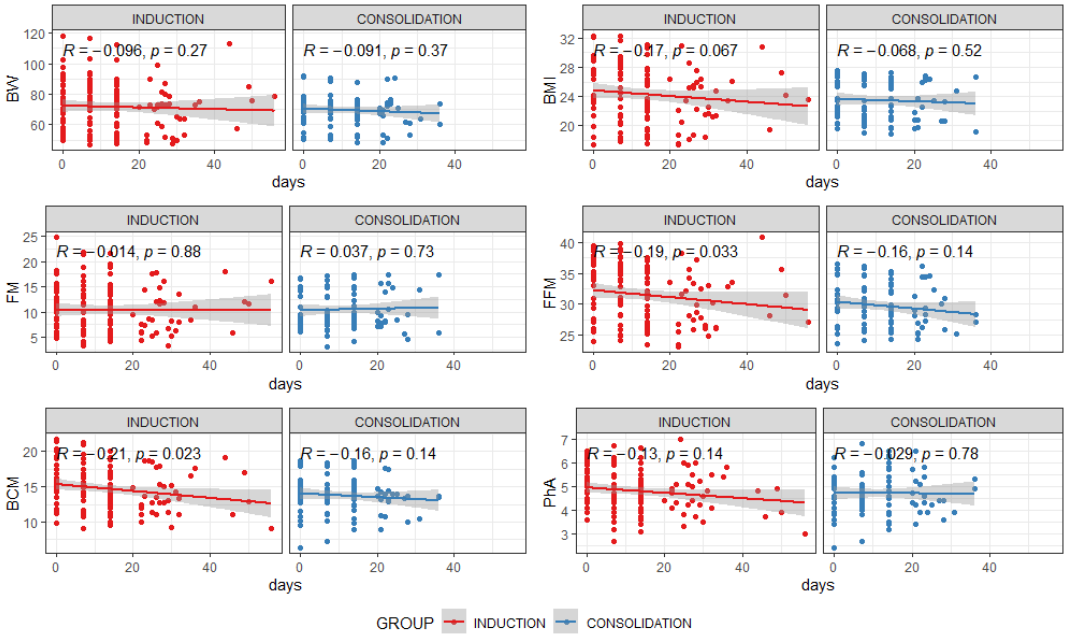

Figure 4. Nutritional status trends during induction and consolidation cycles.

Trends in all anthropometric nutritional parameters (body weight, BW, and body mass index, BMI) and those assessed via BIA (fat mass, FM, fat-free mass, FFM, body cell mass, BCM, and the phase angle, PhA) are shown in **Figure 4**. Data from induction cycles and consolidation cycles are shown separately. Without further stratification, only negative trends of FFM (R = -0.19) and BCM (R = -0.21) during induction chemotherapy cycles are statistically significant. Notably, while a negative trend for BMI can be observed, though not statistically significant, this is even less clear for body weight alone. Even though correlation was found between both FFM and BCM and time during induction cycles, we were not able to show significant differences in any nutritional parameter between time of admission and time of discharge.

For 17 patients, nutritional status could be compared between time of diagnosis, defined “t0”, and time of discharge after two courses of chemotherapy, which was defined as “t60”. A negative trend was seen for all parameters from the first to the second timepoint, but no statistically significant

differences were found (**Figure 5**), even when observations were divided by low vs. high NRS (data not shown).

No clear difference was observed in nutritional status trends when data was analyzed separately based on occurrence of long episodes of fever (lasting seven days or more) or based on NRS-2002 score at diagnosis (high NRS-2002 score was defined as 3 or more), as shown in **Figure 6** and **Figure 7**.

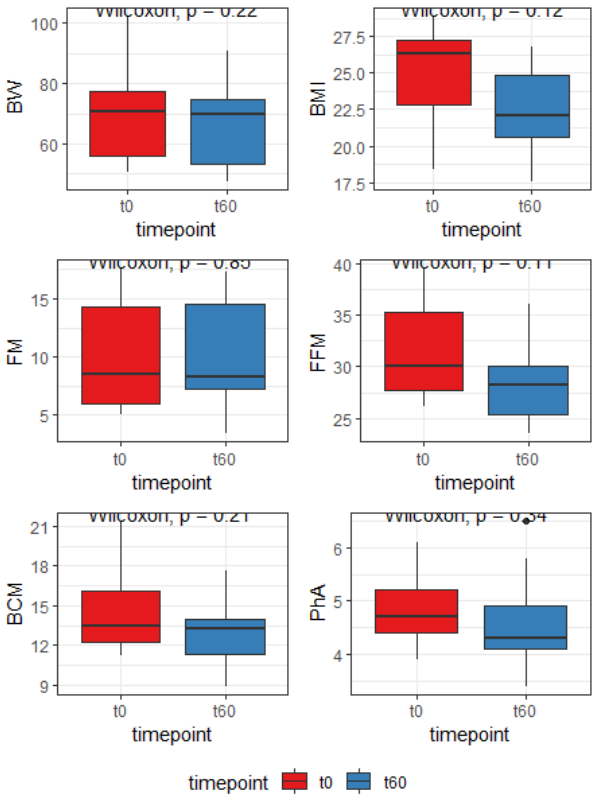

Figure 5. Differences at t0 vs t60.

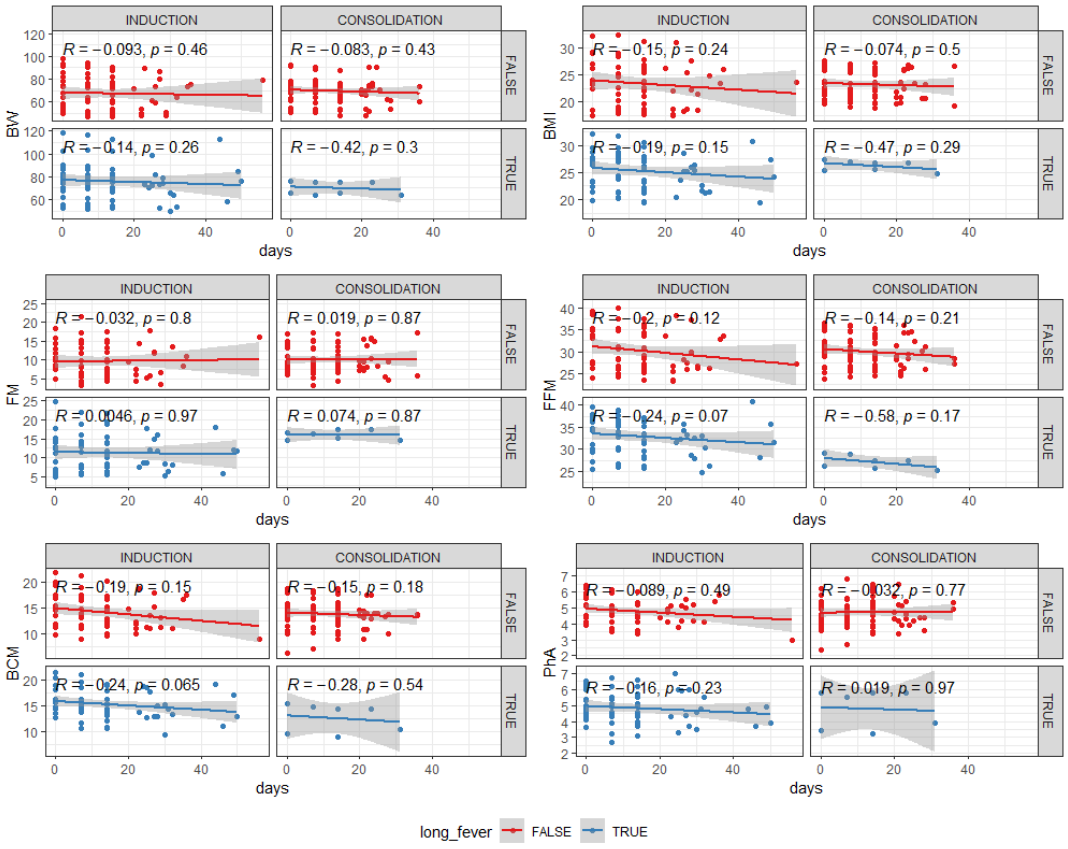

Figure 6. Nutritional status trends based on fever.

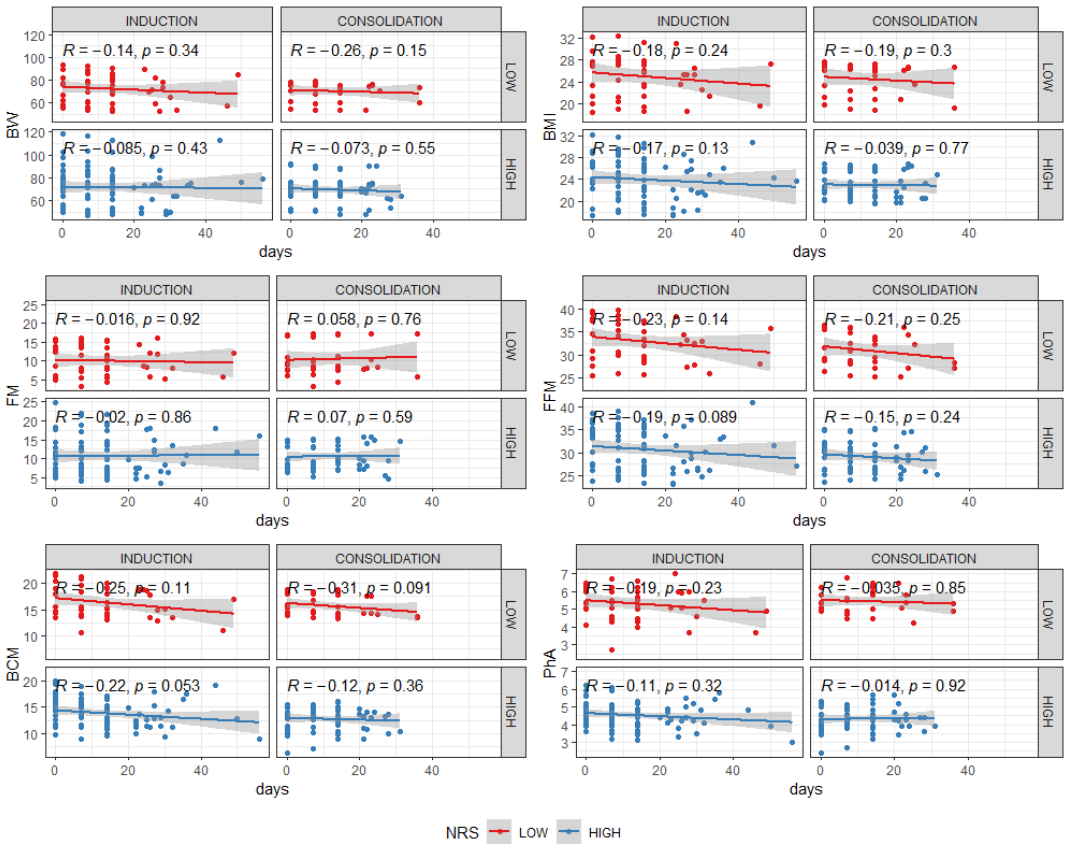

Figure 7. Nutritional status trends based on NRS-2002 at diagnosis.

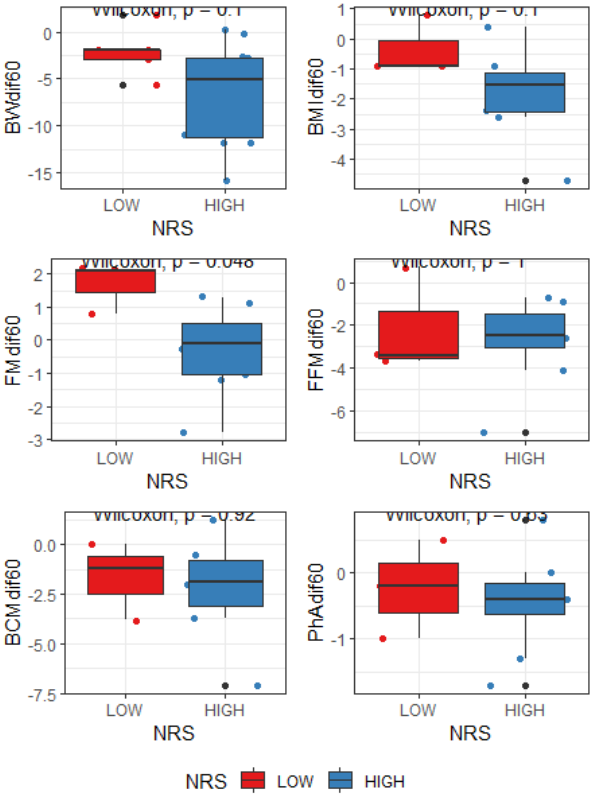

Figure 8. Differences between t0 and t60 by NRS

Difference between nutritional parameter values at t0 and t60 was calculated and defined "dif60". When these differences were analyzed, a trend towards worse nutritional status was observed in general for patients with high NRS-2002, but the only significant difference between the two groups was relative to fat mass, which resulted to have a more pronounced reduction at t60 in patients with high vs. low NRS-2002 (**Figure 8**). No significant differences were found in dif60 even when patients were analyzed by disease response (CR vs. no CR, data not shown).

Predicting nutritional status variation

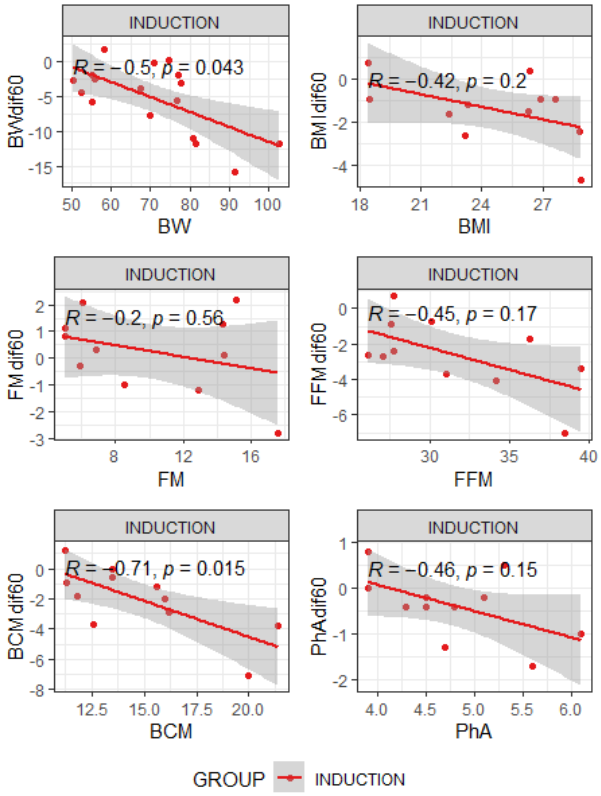

Figure 9. Correlation between nutritional status at time of diagnosis (t0) and after two cycles of chemotherapy (t60).

Correlation between nutritional status at time of diagnosis (t0) and after two cycles of chemotherapy (t60) was tested. In general, a negative trend was observed for all parameters (e.g., patients who weighed more at time of diagnosis were those who lost more weight after two cycles of chemotherapy), but the negative correlation was statistically significant only for BW and BCM (**Figure 9**).

Next, we focused on early variations in nutritional parameters, and tested correlation between variations as early as 7 days (dif7) or 14 days (dif14) after start of chemotherapy and cumulative variation in the same nutritional parameter at discharge after the first (dif30) or after the second (dif60) cycle of chemotherapy. For all parameters a positive correlation was observed between dif7 and dif30, but statistical significance was observed only for FFM (R = 0.58), BCM (R = 0.51 and 0.62 in induction and consolidation, respectively) and PhA (R = 0.5 and 0.59 in induction and consolidation, respectively) both in induction and consolidation cycles. Significant correlation was also found for FM (R = 0.43) only in induction cycles, but no significant correlation was observed for BW or BMI changes (**Figure 10**).

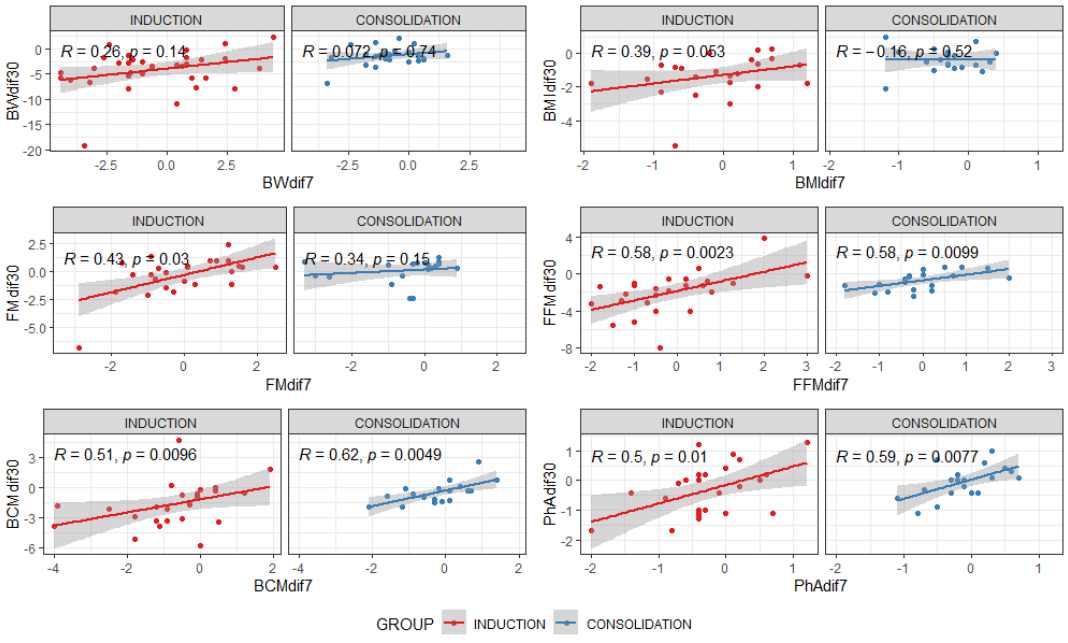

Figure 10. Correlation between variations after 7 days and at discharge.

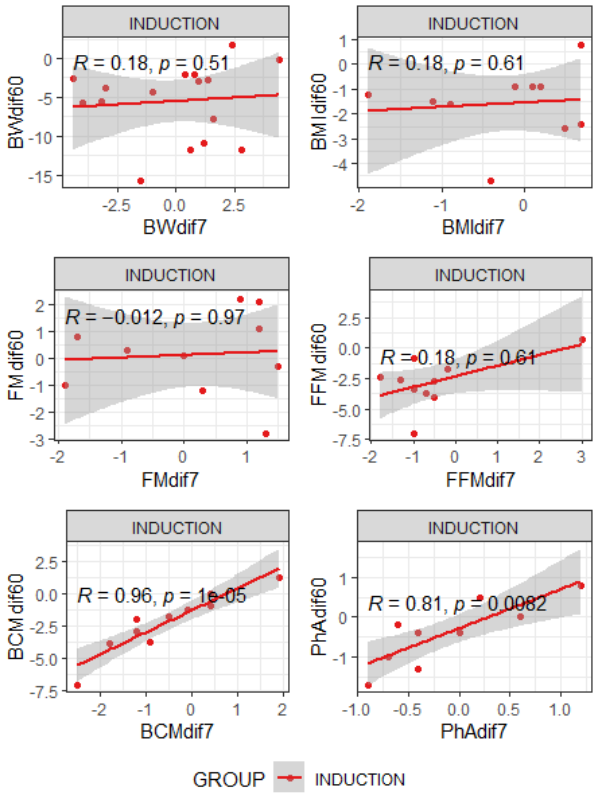

Figure 11. Correlation between variations after 7 days and at discharge after 2 CHT cycles.

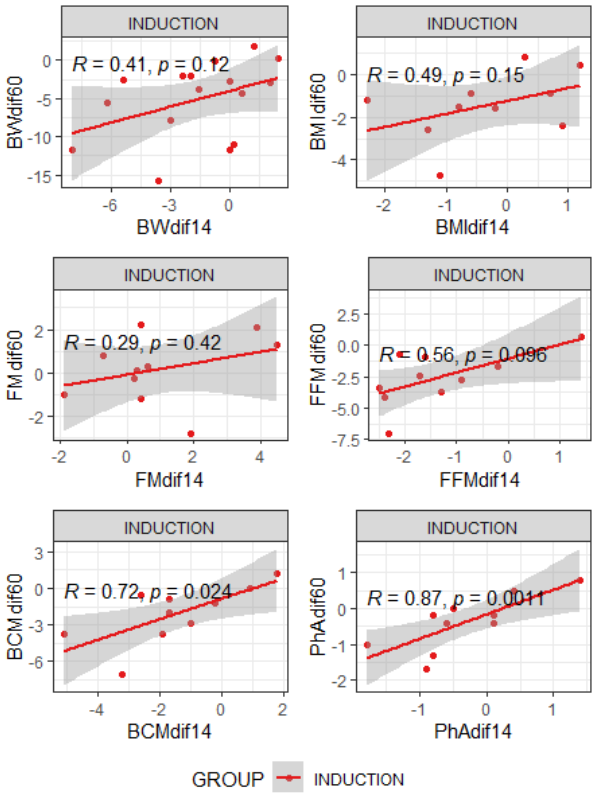

Figure 12. Correlation between variations after 14 days and at discharge after 2 CHT cycles.

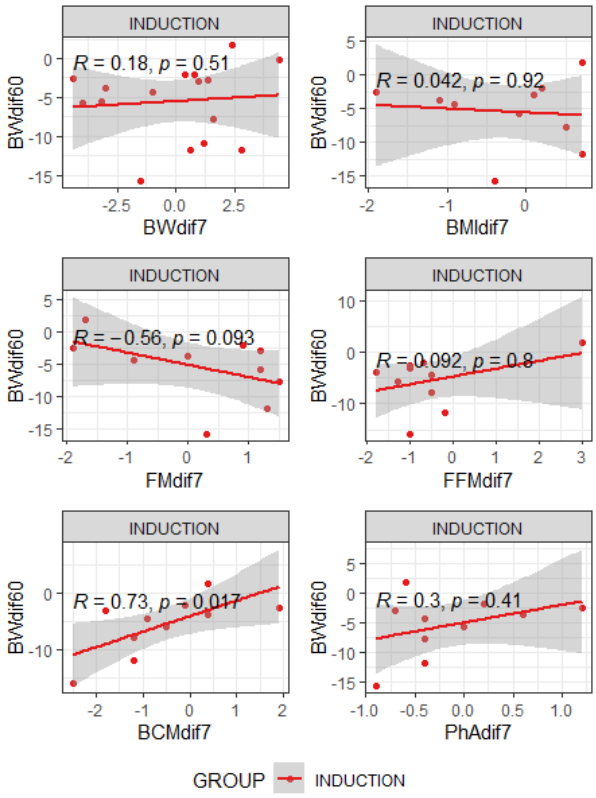

Figure 13. Correlation between dif7 values and BWdif60.

Correlation analysis between dif7 and dif60 confirms a strong association between the two measures for BCM (R = 0.96) and PhA (R = 0.81), again with no significant correlation for BW or BMI (**Figure 11**). Correlation between dif14 and dif60 was also tested. Again, associations were found only for BCM (R = 0.72) and PhA (R = 0.87) (**Figure 12**).

To identify potential early predictors of weight loss along treatment, correlation was tested between values at t0, dif7, or dif14 of all nutritional parameters with BWdif60. For values at t0, only BW correlated with BWdif60 (as already shown). Interestingly, when dif7 values were analyzed, a correlation with BWdif60 was found only for BCM (R= 0.73), while BWdif7 itself was not predictive (**Figure 13**).

No statistically significant correlations were found between dif14 and BWdif60 for any nutritional parameter (data not shown).

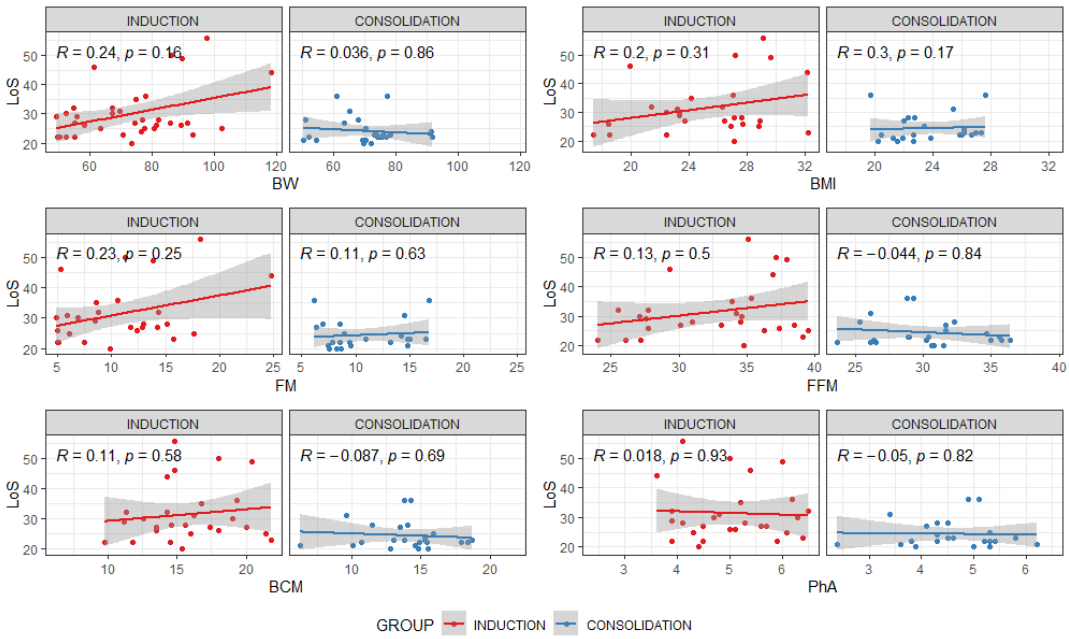

Figure 14. Correlation between nutritional status at admission and length of stay (LoS).

Nutritional status and length of stay

Correlation between nutritional status at admission and length of stay (LoS) was tested, but no significant association was found (**Figure 14**).

Then, potential correlation between early nutritional parameter variations and length of stay was tested. A negative correlation was found for BW (R = -0.48), BMI (R = -0.71) and FM (R= -0.47) at day 7 (**Figure 15**), and a negative correlation was found for PhA (R = -0.6) at day 14 (**Figure 16**), but all correlations were seen only in consolidation CHT cycles.

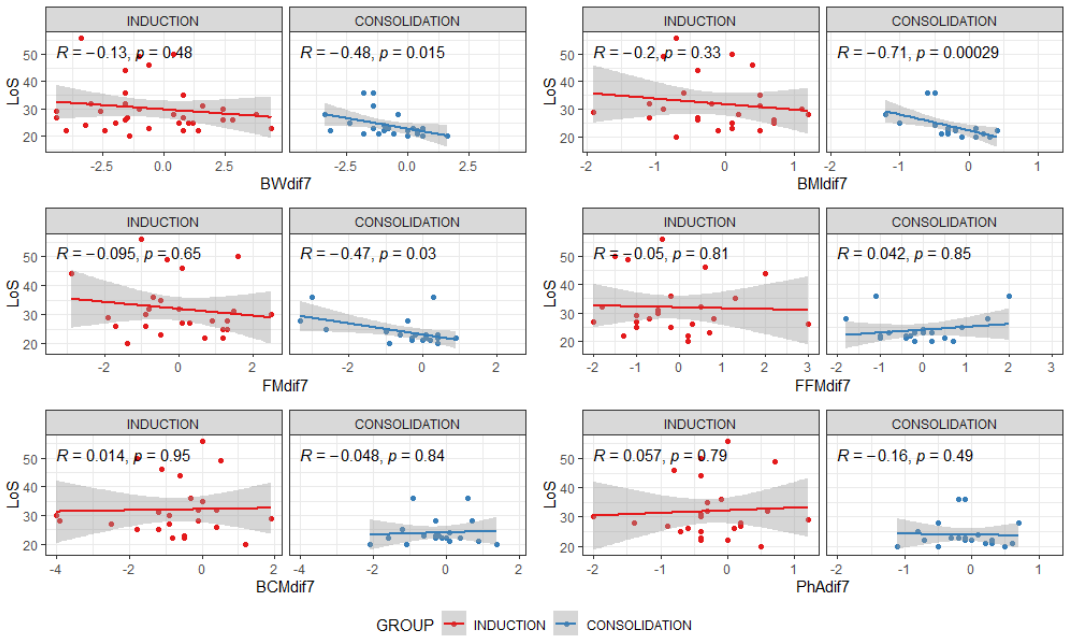

Figure 15. Analysis of correlation between nutritional parameter variation at day 7 and length of stay.

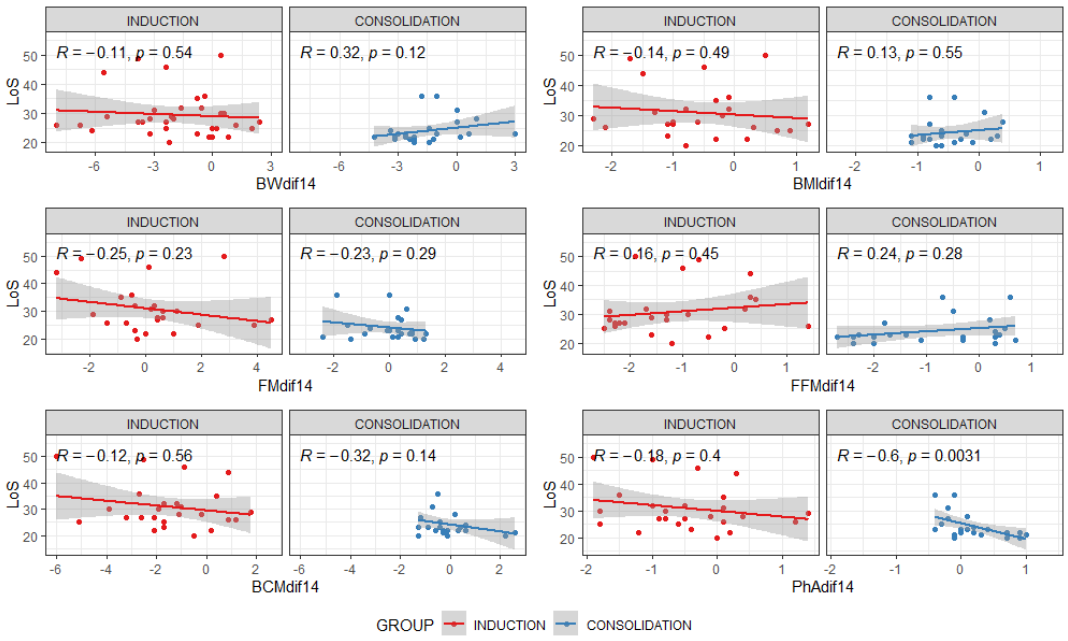

Figure 16. Analysis of correlation between nutritional parameter variation at day 14 and length of stay.

Nutritional status and response to therapy

Finally, nutritional status at time of diagnosis and nutritional status variations at early timepoints were tested for associations with response to therapy. No significant association was found for any parameter (**Figure 17** and **Figure 18**).

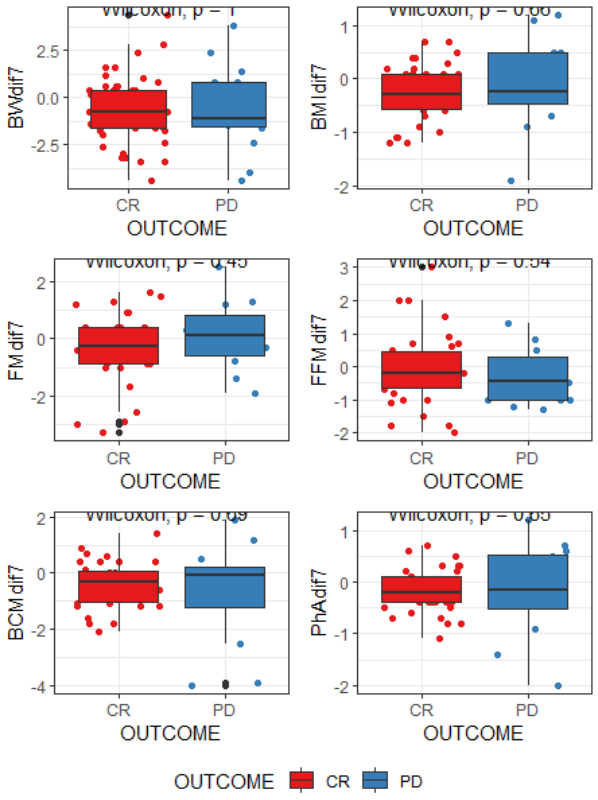

Figure 17. Analysis of correlation between nutritional parameter variation at day 7 and response to therapy.

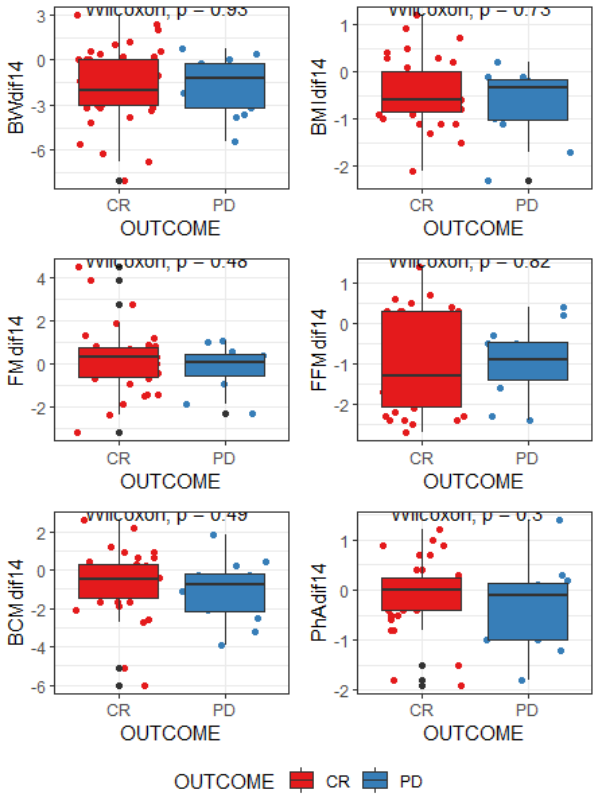

Figure 18. Analysis of correlation between nutritional parameter variation at day 14 and response to therapy.

Discussion

Fit patients diagnosed with acute myeloid leukemia are conventionally treated with repeated cycles of intensive chemotherapy, often followed by allogeneic hematopoietic stem cell transplant. Intensive treatment, albeit effective, carries a toxicity burden, which often limits the full application of the therapeutic program reducing its potential efficacy.

Progress has been made on many fields (infection prophylaxis and cure, particularly for fungal infections, prevention and treatment of nausea), but nutritional toxicity is still very common, especially for patients with AML, who are usually subject to long, repeated hospitalization. Additionally, these patients are usually prescribed a neutropenic diet to prevent GI infections, with consequent further reduction in nutritional intake.

While international guidelines are available for nutritional monitoring and support in patients with cancer,[8] nutritional guideline implementation and application are still limited for hematologic patients, which present several key differences compared with non-hematologic patients (more frequent cytopenias, infections and mucositis).[14–18]

With the help of a trained dietitian, at our institution we now assess nutritional status of patients with AML hospitalized and treated with intensive chemotherapy. Nutritional data (including BIA, anthropometric parameters, and biochemical parameters) is prospectively collected during all cycles of chemotherapy.

Here, we present preliminary results from the first 21 patients included in the study, whose nutritional data was analyzed and recorded during a total of 61 chemotherapy cycles. A limitation of this analysis is the relatively small sample size and short follow up (300 days), which do not allow to test associations of nutritional data with survival. Still, a few interesting findings will be discussed.

Nutritional risk scores are routinely calculated at time of hospitalization for any reason, including for cancer patients admitted for chemotherapy. Risk scores are validated and used to predict the risk of malnutrition, but most cancer patients, especially those with particularly aggressive disease such as AML, are at high risk at time of diagnosis. In our sample, median Nutritional Risk Score 2002 (NRS) score was 3, but the score allocates 2 points to all patients with AML. Thus, only 9 patients (35%) had low NRS, while the remaining 65% were at high risk. Moreover, when nutritional parameters and their variation were analyzed stratifying patients for high vs. low NRS, only a more pronounced reduction in fat mass (but not in body cell mass) was found after two cycles of chemotherapy. In other words, in our population NRS only predicted a reduction in fat mass, but not in the metabolically active, muscular mass.

In fact, when anthropometric parameters and those obtained by bioelectrical impedance analysis were analyzed together, we found that a general negative trend could be observed for all these parameters, but it was more evident for FFM and BCM (less clear for BW and BMI) during induction chemotherapy cycles. A reason for this may be that body weight (and BMI) is affected by several factors especially during hospitalizations for induction chemotherapy: high volumes of fluids need to be administered to prevent tumor lysis syndrome and, later, as fluid resuscitation for sepsis, which is a common complication in this subset of patients. Thus, a more sensitive technique that can discriminate fluids and fat from the metabolically active part of body mass holds promise to provide more precise estimates of the actual nutritional status of such delicate patients. It is expected,

though, that as sample size will increase, negative trends in BW and BMI will become significant at least for induction chemotherapy cycles. This would be in line with findings already reported in the literature.[17,18]

At t0 (admission for induction chemotherapy) values of BW and BCM both negatively correlated with variations in BW and BCM at t60 (at discharge after two cycles of chemotherapy), but correlation was better for BCM (R = -0.71, p = 0.015) compared with BW (R = -0.5, p = 0.043). Variations of FFM, BCM and PhA 7 days after admission were already associated with cumulative variations in the same parameter at discharge after either an induction or consolidation chemotherapy cycle. For BCM and PhA, correlations were also evident between variations 7 days after admission for induction chemotherapy and cumulative variation at discharge after two cycles of consolidation (t60). No correlations were seen for classic anthropometric parameters. In other words, variations in a single nutritional parameter as early as 7 days after admission for induction chemotherapy are associated with variations in the same parameter two months later.

More interestingly, while body weight loss at day 7 of induction chemotherapy did not show any association with cumulative body weight loss after two cycles (R = 0.18, p = 0.51), we found a statistically significant correlation between BCM variation at day 7 of induction chemotherapy and cumulative weight loss after two cycles (R = 0.73, p = 0.017). While this finding needs confirmation in a larger cohort, early variation in BCM may be a predictor of weight loss in the medium-long term.

No meaningful association was found between nutritional status monitored as described and length of stay or response to therapy. A longer follow up and larger sample size will be needed to analyze effect of nutritional status on survival. A recent study found a correlation between baseline values of phase angle and both overall and progression-free survival, which was confirmed in multivariable analysis.[19]

Additionally, analysis of the effect of nutritional risk scores more recently developed (PNI, CONUT) and of different chemotherapy cycles (e.g., 3+7, vs. fludarabine-based) on nutritional status will be carried out when numbers will allow it.

Nutritional assessment by bioelectrical impedance analysis could allow clinicians to identify early signs of malnutrition, which may become evident before and more reliably than weight loss. Additional biological correlations, for example with microbiome, which has been closely correlated with nutrition[20,21], may give even more granular information on the patients and their nutritional and immunological status.

More precise information may be coupled with early nutritional intervention, which is much wider than in the past and includes nutritional therapy, such as prescription of oral nutritional supplements or artificial nutrition, but also physical therapy and psychological support.

Preliminary results presented here are a first step towards a “comprehensive” nutritional approach which is being developed and carried out at our institution, with the final goal of reducing nutritional and overall toxicity for patients affected by acute myeloid leukemia.

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