



# May nutritional status worsen during hospital stay? A sub-group analysis from a cross-sectional study

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## Abstract

Hospital malnutrition is a detrimental prognostic factor regarding hospital mortality, complications, and length of stay. However, the role of hospitalization itself on nutritional status has not been fully elucidated. We report the results of a secondary analysis from the dataset of a recent cross-sectional study at Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. Data from patients evaluated at admission and discharge were collected and compared. One hundred thirty-nine patients were evaluated. Mean length of stay was 13.6 ( $\pm 7.7$ ) days. Patients at risk of malnutrition, according to NRS-2002, were 75 (53.9%), while 63 (45.3%) were malnourished according to ESPEN Criteria. Compared to admission, at discharge, patients reported a significant decrease in Mid-Upper Arm Circumference (MUAC)—from 26.5 cm ( $\pm 3.6$ ) to 25.9 cm ( $\pm 3.7$ ) ( $p=0.016$ ), a reduction in Phase angle (PhA)—from 4.25° ( $\pm 1.20$ ) to 4.01° ( $\pm 1.15$ ) ( $p=0.005$ ), fat-free mass (FFM)—from 47.5 kg ( $\pm 9.19$ ) to 44.9 kg ( $\pm 9.4$ ) ( $p=0.03$ ) and fat-free mass index (FFMI)—from 16.9 kg/m<sup>2</sup> ( $\pm 2.3$ ) to 15.8 kg/m<sup>2</sup> ( $\pm 2.7$ ) ( $p=0.04$ ). Laboratory data showed a reduction of albumin—from 29.2 ( $\pm 5.7$ ) to 28.0 ( $\pm 5.9$ ) ( $p=0.01$ ) and Onodera's PNI—from 29.1 ( $\pm 5.6$ ) to 27.6 kg ( $\pm 5.6$ ) ( $p=0.039$ ). At the multivariate linear regression analysis, the variables significantly associated with a worsening of PhA at discharge are the PhA value at admission and the diagnosis of malnutrition according to ESPEN Criteria. Hospitalization leads to significant changes in nutritional status. A clinical concern should be raised about the quality of hospital food and meal times and on the need for a clinical nutritionist on the ward.

**Keywords** Nutritional status · Hospital malnutrition · Phase angle · Fat-free mass · Prognostic nutritional index · ESPEN criteria · Personalized medicine

## Introduction

Hospital malnutrition is a well-known problem, influencing hospital stay with clinical and socioeconomic consequences. There is much evidence showing the impact of poor nutritional status on clinical outcomes, such as length of hospital stay (LOS), morbidity, and mortality [1, 2].

Given the high prevalence of malnutrition in hospital wards [3], a nutritional assessment should be mandatory from the time of admission. Many efforts have been made to implement nutritional care during hospital stay, such as the appropriateness of meals, the use of oral nutritional supplements (ONS) and the correct nutritional route in patients not able to eat (i.e., enteral or parenteral nutrition) [4–6]. Recent evidence highlights the cost-effectiveness of the application of nutritional support on hospital and clinical outcomes, such as length of stay, survival, and money-savings [7, 8]. Nevertheless, the importance of this matter

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seems to continue to be underestimated in clinical practice and the burden of hospital malnutrition as yet is not sufficiently valued and managed on a large scale [9].

Moreover, the impact of hospitalization itself on patient's nutritional status has not been fully elucidated. Given the inflammatory and catabolic state of all acute and/or chronic illnesses and cancer diseases (leading to a loss of lean and fat body mass), it is plausible that there would be a worsening of nutritional status during hospital stay [10, 11]. This is highly probably on an Internal Medicine and Gastroenterology Unit, for the high rate of comorbidities, the high prevalence of age-related sarcopenia and metabolic diseases [12]. However, this hypothesis needs to be tested.

In our recent cross-sectional study, conducted on 300 patients of the Internal Medicine and Gastroenterology Department of a Tertiary Care Referral University Hospital (Fondazione Policlinico A. Gemelli IRCCS, Rome), we show a rate of 52.3% of patients at risk of malnutrition and a rate of 38.7% malnourished patients. We also find that malnourished patients have a mean LOS 2 days longer than nourished ones [13].

The aim of this work is to perform a sub-group analysis of the study mentioned above, regarding those patients who received a nutritional assessment both at admission and at discharge, to compare their nutritional status before and after the hospital stay.

## Methods

This is a sub-group, secondary analysis of the dataset from an observational study, performed at Fondazione Policlinico Universitario A. Gemelli in Rome, between March and December 2017 [13]. All patients received a nutritional evaluation within 72 h of admission as for clinical practice in our center (see below). The previous study was a cross-sectional study, in which all patients (> 18 years old) admitted in the Internal Medicine and Gastroenterology Unit, and giving their consent, were included. Patients not suitable for evaluation, i.e., not conscious or with the failure of at least one vital organ, were excluded. Patients hospitalized for a programmed procedure and discharged within 4 days were excluded for reasons regarding the primary analysis (estimation of the length of stay according to nutritional status). Many patients also received at discharge a second evaluation, requested by the ward physician, to give them a nutritional home plan. Data from patients having a nutritional evaluation both at admission and at discharge were selected for this secondary analysis.

As previously discussed, the nutritional risk at admission was calculated according to Nutritional Risk Screening 2002 (NRS-2002), endorsed by the European Society for Clinical Nutrition and Metabolism (ESPEN) [14]. A score < 3

stands for “no nutritional risk,” whereas a score  $\geq 3$  identifies patients at risk, deserving a nutritional assessment and care plan. Nutritional assessment was performed according to ESPEN Criteria, recently released from ESPEN Society and already validated in clinical settings [3, 15]. Height in meters (m) and weight in kilograms (kg) were calculated using a professional balance beam scale with height rod (Seca 700 Physician's Balance, Seca®). In bedridden patients, weight was obtained using bed-integrated weighing scale (Hill-Rom® 1000 Medical Surgical bed) and height estimated from ulna length, according to the table released by the British Association for Parenteral and Enteral Nutrition (BAPEN) [16]. BMI was calculated as weight divided by height squared ( $\text{kg}/\text{m}^2$ ). Body circumferences were obtained according to accepted standards [17]. Bioelectrical Impedance Analysis (BIA) was carried out with a multi-frequency device (BodyStat© 4000, BodyStat LTD) on patients lying down supine on the bed, with arms not touching the torso and legs not touching at the thigh, according to the accepted standards [18]. Resistance (R) and Reactance (Xc) at the frequency of 50 kHz were obtained. The software calculates Phase Angle (PhA) according to the formula:

$$\text{PhA} = \arctan(Xc/R) \times (180/\pi)$$

Fat mass (FM) and fat-free mass (FFM) were derived, according to Company equations. FM index (FMI) and FFM index (FFMI) were then calculated by dividing FM and FFM by the square of the patient's height in meters ( $\text{kg}/\text{m}^2$ ). Handgrip strength test (HGS) was performed using a hand dynamometer (DynEx™ 12-0455 Digital Hand Grip, Akern Srl) according to the accepted standards [19]. A total of three measures were obtained from each patient, and the mean HGS was calculated. Demographic and laboratory data, main admission diagnoses and comorbidities were also collected. The Charlson Comorbidity Index (CCI) [20] was calculated for each patient.

Data from patients having a nutritional evaluation both at admission and at discharge were selected for statistical analysis. Anthropometrical data (body circumferences, weight, BMI), HGS, bioelectrical impedance and laboratory values were collected and compared as paired data. Onodera's Prognostic Nutritional Index (PNI) was calculated according to the formula:

$$10 \times \text{Albumin (g/dl)} + 0.005 \times \text{total lymphocyte count} (\times 10^9/\text{l}) [21].$$

The length of stay was calculated (in days) from admission to discharge day.

The research was carried out according to the Declaration of Helsinki and obtained the approval of the Institutional Review Board and Ethics Local Committee (Protocol Number 53572/17).

Statistical analysis was performed using STATA® Software (Version 14.0, Stata Corporation; College Station,

TX, USA). Continuous variables were summarized using mean  $\pm$  standard deviation, categorical data using frequency counts (percentage). Kolmogorov–Smirnov test was used to evaluate if the continuous variables had a normal distribution. A paired Student's *t* test was used to compare continuous variables in two groups. A multivariate linear regression was performed to avoid possible confounder elements for decreases of PhA. Type I ( $\alpha$ ) error was set at 0.05. Statistical significance was defined when  $p < 0.05$  (two-tailed).

## Results

All patients evaluated gave their consent to the data analysis and report. Five patients were excluded from analysis as not suitable, according to selection criteria (see above). Between February and November 2017, one hundred and thirty-nine patients, admitted from the Emergency Department for an acute condition, have been evaluated both on admission and at discharge. Seventy-six (54.7%) were

male; the mean age was 62.6 ( $\pm 17.6$ ). Fifty patients (36%) were affected by cancer (liver 35%, pancreas 33%, colon 12%, others 20%); 24 patients (17%) were affected by liver cirrhosis (50% Child A, 30% Child B, 20% Child C); 14 (10.1%) by cholangitis or other biliary pathology (the complete list of diagnoses is reported in Table 1). Mean length of stay was 13.6 ( $\pm 7.7$ ) days. Patients at risk of malnutrition, according to NRS-2002 were 75 (53.9%), while the malnourished ones according to ESPEN Criteria were 63 (45.3%) (Table 1). Compared to admission, at discharge weight and BMI did not significantly differ, even if patients reported a slight but significant decrease in MUAC, from 26.5 cm ( $\pm 3.6$ ) to 25.9 cm ( $\pm 3.7$ ) ( $p = 0.016$ ). There was also a significant reduction in PhA—from 4.25° ( $\pm 1.20$ ) to 4.01° ( $\pm 1.15$ ) ( $p = 0.005$ ), FFM—from 47.5 kg ( $\pm 9.19$ ) to 44.9 kg ( $\pm 9.4$ ) ( $p = 0.03$ ) and FFMI—from 16.9 kg/m<sup>2</sup> ( $\pm 2.3$ ) to 15.8 kg/m<sup>2</sup> ( $\pm 2.7$ ) ( $p = 0.04$ ). No significant changes have occurred in FM and FMI. Laboratory data showed a reduction of albumin—from 29.2 ( $\pm 5.7$ ) to 28 ( $\pm 5.9$ ) ( $p = 0.01$ ), and Onodera's PNI—from 29.1 ( $\pm 5.6$ )

**Table 1** Demographical data, main diagnoses and baseline characteristics of admitted patients

Total (139 patients)		
	Mean	SD
Age	62.6	$\pm 17.6$
Total (139 patients)		
	Number	%
Male sex	76	54.7
Admission diagnoses		
Cancer (overall)	50	36
Cirrhosis (any stage)	24	17.4
Biliary pathology	14	10.1
Anemia (overall)	10	7.2
Cardiovascular diseases	8	5.7
Others (gastrointestinal diseases)	8	5.7
Infections	6	4.3
Inflammatory bowel diseases	5	3.6
Acute pancreatitis	5	3.6
Upper gastrointestinal diseases	5	3.6
Acute alcohol intoxication	2	1.4
Others (non-gastrointestinal diseases)	2	1.4
Charlson Comorbidity Index		
CCI 1	46	33.1
CCI 2	40	28.8
CCI 3	29	20.8
CCI 4	24	17.3
NRS-2002 $\geq 3$	75	53.9
Malnourished according to ESPEN Criteria	63	45.3

SD standard deviation, CCI Charlson Comorbidity Index, NRS-2002 Nutritional Risk Screening-2002, ESPEN European Society for Clinical Nutrition and Metabolism

to 27.6 kg ( $\pm 5.6$ ) ( $p = 0.039$ ). Complete data are reported in Table 2.

Multivariate linear analysis (Table 3) shows that a PhA reduction at discharge is associated both with PhA values [Coefficient (95% CI): 0.647 (0.520–0.773);  $p < 0.001$ ] and with diagnosis of malnutrition (according to ESPEN criteria) at admission [ $-0.382$  ( $-0.634$  to  $-0.131$ );  $p = 0.003$ ]; other covariate's elements tested (CCI classes, LOS, age, sex, Onodera's PNI) show no statistical association with PhA worsening (Adjusted  $R$ -squared of the model: 0.72;  $p < 0.001$ ).

## Discussion

Hospital malnutrition represents a detrimental variable for hospital outcomes. Our Hospital Governance requests to researcher and clinicians to implement every effort towards a personalized medicine. Since nutritional care is a model

**Table 2** Comparison between admission and discharge values among paired patients

Total (139 patients)			
	Admission	Discharge	$p$
	Mean (SD)		
<b>Anthropometrical data</b>			
Weight (kg)	67.1 ( $\pm 13.5$ )	66.5 ( $\pm 13.4$ )	0.22
BMI (kg/m <sup>2</sup> )	23.8 ( $\pm 4.5$ )	23.6 ( $\pm 4.5$ )	0.22
Wrist (cm)	16.6 ( $\pm 1.3$ )	–	–
Waist (cm)	90.6 ( $\pm 14.3$ )	89.3 ( $\pm 15.4$ )	0.23
Hip (cm)	93.2 ( $\pm 11.6$ )	93.4 ( $\pm 9.1$ )	0.79
MUAC (cm)	26.5 ( $\pm 3.6$ )	25.9 ( $\pm 3.7$ )	0.016
Handgrip Strength test (kg)	19 ( $\pm 9.3$ )	18.8 ( $\pm 9.5$ )	0.52
<b>Bioelectrical impedance values</b>			
PhA (°)	4.25 ( $\pm 1.20$ )	4.01 ( $\pm 1.15$ )	0.005
FFM (kg)	47.5 ( $\pm 9.19$ )	44.9 ( $\pm 9.4$ )	0.03
FFMI (kg/m <sup>2</sup> )	16.9 ( $\pm 2.3$ )	15.8 ( $\pm 2.7$ )	0.04
FM (kg)	20.8 ( $\pm 6.8$ )	20.4 ( $\pm 8.4$ )	0.38
Fat mass index (kg/m <sup>2</sup> )	7.4 ( $\pm 2.5$ )	7.3 ( $\pm 3.2$ )	0.53
<b>Laboratory data</b>			
Hemoglobin (g/dl)	11.1 ( $\pm 2.3$ )	10.8 ( $\pm 1.8$ )	0.08
WBC ( $\times 10^9/l$ )	9.95 ( $\pm 6.56$ )	8.74 ( $\pm 5.76$ )	0.016
Lymphocytes ( $\times 10^9/l$ )	1.41 ( $\pm 0.66$ )	1.54 ( $\pm 0.76$ )	0.036
Creatinine (mg/dl)	0.97 ( $\pm 0.56$ )	0.93 ( $\pm 0.55$ )	0.39
Albumin (g/l)	29.2 ( $\pm 5.7$ )	28 ( $\pm 5.9$ )	0.01
CRP (mg/l)	76.9 ( $\pm 85.4$ )	44.1 ( $\pm 53.6$ )	0.004
Onodera's PNI	29.1 ( $\pm 5.6$ )	27.6 ( $\pm 5.6$ )	0.039

*SD* standard deviation, *MUAC* mid-upper arm circumference, *PhA* phase angle, *FFM* fat-free mass, *FFMI* fat-free mass index, *FM* fat mass, *FMI* fat mass index, *WBC* white blood cells, *CRP* C-reactive protein, *PNI* prognostic nutritional index

**Table 3** Multivariate linear regression on PhA values at discharge

	Coefficient (95% CI)	$p$
Phase Angle at admission	0.647 (0.520–0.773)	<0.0001
Charlson comorbidity index:		
CCI 1	1	–
CCI 2	$-0.041$ ( $-0.354$ to $0.273$ )	0.79
CCI 3	$-0.098$ ( $-0.432$ to $0.234$ )	0.56
CCI 4	$-0.076$ ( $-0.456$ to $0.304$ )	0.69
LOS (days)	$-0.003$ ( $-0.018$ to $0.013$ )	0.71
Age	$-0.008$ ( $-0.016$ to $0.010$ )	0.06
Diagnosis of malnutrition according to ESPEN Criteria at admission	$-0.382$ ( $-0.634$ to $-0.131$ )	0.003
Sex	$-0.183$ ( $-0.435$ to $0.068$ )	0.15
Onodera's PNI at admission	$0.022$ ( $-0.002$ to $0.046$ )	0.07

*CCI* Charlson comorbidity index, *LOS* length of stay, *ESPEN* European Society for Clinical Nutrition and Metabolism, *PNI* prognostic nutritional index

\*Adj.  $R$ -squared: 0.72;  $p < 0.0001$

of personalized medicine, every patient admitted in Internal Medicine and Gastroenterology Unit receives a nutritional assessment within 72 h from admission.

Our sub-group analysis, conducted in the Internal Medicine and Gastroenterology Department of a Tertiary Care Referral University Hospital, in Italy, shows a significant worsening of patients' nutritional status during hospitalization, measured as a reduction in PhA, FFM and FFMI values at the time of discharge. On the contrary, no weight, BMI, and FM changes have been recorded. Recently, PhA has been reported as a prognostic nutritional index of body composition [22]; low PhA values have been correlated with worse prognosis regarding survival, postoperative complications and LOS in several clinical settings [13, 23, 24]. Indeed, it is endorsed as a nutritional prognostic marker by ESPEN Society. Even if sarcopenia is not accurately measured by BIA—in the clinical practice dual X-ray absorptiometry (DXA) and computed tomography (CT) scan are the gold standard techniques—a low BIA-derived FFMI is associated with poor outcome in terms of LOS when compared with normal FFMI in a large cohort of hospital patients [25, 26].

Interestingly, even if the lymphocyte count increases from admission to discharge, Onodera PNI shows a slight but significant worsening. Onodera PNI is a simple nutritional index composed of the albumin and lymphocyte counts. It was released in 1984 as a prognostic nutritional index regarding overall survival for malnourished cancer patients undergoing gastrointestinal surgery [21]. Its prognostic nutritional value was recently confirmed in many clinical settings: a low PNI is correlated with worse survival, postoperative complication and chemotherapy-associated toxicities [27–29]. However, we recognize the limited value of

albumin in this setting, given the short-term re-evaluation (mean LOS  $13.6 \pm 7.7$  days), which is inferior to the mean albumin serum half-life (25 days). Moreover, a possible sampling bias could be present, having no information regarding intravenous albumin supplementation.

All in all, such body composition alterations occurred in a mean time of 13.3 days; we could argue that in a longer period we could have observed more severe nutritional alterations (weight, BMI, FMI, HGS).

At the multivariate linear regression analysis, the variables significantly associated with a worsening of PhA at discharge are the PhA value at admission and the diagnosis of malnutrition according to ESPEN Criteria. The impact of other clinical covariates, such as CCI, age, LOS, gender, or Onodera's PNI is not statistically significant. These results justify the need for a bioelectrical impedance assessment of every patient at hospital admission and outline the value of application of ESPEN Criteria to find malnourished patients.

Our results are in line with a recent multi-centric Chinese hospital study (34 hospitals), evaluating 2328 cancer patients at admission and discharge, from June to September 2014. In this study, the authors find a higher rate of patients at risk of malnutrition at discharge vs. admission (NRS-2002  $\geq 3$ : 58.1% vs. 51.7%;  $p < 0.001$ ), with BMI, body weight, grip and calf circumferences significantly decreased at the time of discharge, compared with admission ( $p < 0.05$ ) [30].

There are many reasons for the worsening of nutritional status in hospitalized patients. First of all, the inflammatory status due to the acute/chronic baseline disease: it has been frequently demonstrated the impact of systemic inflammation in generating anorexia, fatigue, pain, and weight loss. This cohort of signs and symptoms is due to metabolic derangements, such as elevating resting metabolic rate, insulin-resistance, lipolysis, and proteolysis, driven by inflammatory cytokines like tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interferon- $\gamma$  (IFN- $\gamma$ ) or interleukin-1 (IL-1). Until restored, this state leads to lean body mass and fat mass wasting [31].

A second important point is the poor hospital food intake—associated with patient anorexia—giving a high rate of food waste on the hospital wards. In 2012, a survey conducted in a Tertiary care center in Amsterdam, The Netherlands, found that almost 40% of the food provided by the hospital kitchen was wasted. As a consequence, in spite of the energy requirements provided by the hospital food ( $1809 \pm 143$  kcal and  $76 \pm 13$  g of protein per day, divided into three meals), the effective daily energy and protein amount provided to patients was lower ( $1105 \pm 594$  kcal and  $47 \pm 27$  g of protein per day). [32] To confirm, a recent nursing study reports a mean energy intake of  $669.0 \pm 573.9$  kcal/day/patient, and mean protein intake of  $30.7 \pm 25.8$  g/day/patient in older adult ( $> 65$  years) admitted to an Italian hospital. Over 60% of patients were found to ingest  $\leq 50\%$  of their calculated energy and protein

requirements. Moreover, these patients had longer hospital stays ( $p \leq 0.04$ ) and higher in-hospital and 30-day post-discharge mortality ( $p < 0.001$ ) [33] A significant association between hospital mortality and low caloric and protein intake is further confirmed in another recent prospective observational study on 595 patients affected by acute kidney disease. [34].

There are several different reasons for reduced food intake during the hospital stay. First of all, the patient's clinical condition: many patients report fatigue, swallowing difficulties, impaired self-feeding, cognitive problems, depression, and anorexia. In the lack of a personal caregiver, many of these patients cannot meet the daily energy requirements; many times, in a medical ward, nurses are insufficient to cover this need. Other issues are food quality (not tasty, over or undercooked) and quantity (too small or too large portions). Indeed, it has been reported that up to 75% of patients are unsatisfied with hospital foods [35]. Food presentation and packaging are also important. It has been demonstrated that an inviting meal presentation increases food intake reducing food wasting and decreases hospital readmission rate. [36]. Moreover, meal times are often inappropriate. For example, in many Italian hospitals (our hospital included), dinner is served at half past six in the afternoon, while breakfast is served at 8.00 a.m. So, there are over 13 h of fasting which could be detrimental, especially for patients with a high metabolic rate, cancer patients or patients affected by chronic liver disease, like those admitted to an Internal Medicine ward. It has been calculated that overnight fasting in a cirrhotic patient corresponds to a period of 72 h fast seen in a non-cirrhotic patient [37]. This should raise a concern about hospital meal times.

We must recognize the limitations of our study as a secondary analysis of observational data already collected. For example, we did not perform a sample size analysis to investigate the worsening of nutritional status. Our evidence is based on a pre- and post-analysis of paired data, the second being collected by ward physicians' requests. More methodologically robust studies are needed to confirm our evidence. However, this study could be a warning for the clinicians to recognize the impact of hospitalization on patient's nutritional status and a further stimulus to investigate other possible associated factors and treatments.

In conclusion, we demonstrate that patients' nutritional status (MUAC, FFMI, PhA, Onodera's PNI) may worsen during hospital stay. Factors associated with a nutritional status worsening are PhA at admission and to be already malnourished according to ESPEN Criteria. To pay attention to these variables could be crucial for hospital prognosis and also for patients' recovery after discharge.

Physicians should be aware of the consequence of hospitalization on patients' nutritional status: a nutritional evaluation should be mandatory since from the admission.

A clinical nutritionist should be present among physicians on their rounds. Moreover, a change in hospital meal times and meal quality and presentation should be raised among hospital health management.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Statement of human and animal rights** The study was carried out according to Declaration of Helsinki and obtained the approval of the local Ethics Committee (Fondazione Policlinico A. Gemelli). Protocol number 53572/17.

**Informed consent** Patients gave their informed consent to participate to the survey.

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