

## Original Research

# The Association of Geriatric Nutritional Risk Index and Total Lymphocyte Count with Short-Term Nutrition-Related Complications in Institutionalised Elderly

Emanuele Cereda, MD, Chiara Pusani, RD, Daniela Limonta, MD, Alfredo Vanotti, MD

*International Center for the Assessment of Nutritional Status (ICANS), University of Milan (E.C.), Milan, Servizio di Nutrizione Clinica e Dietetica, ASL Como (C.P., A.V.), Fondazione casa di riposo Dottor Luigi e Regina Sironi - ONLUS, Oggiono - Como (D.L.), Como, ITALY*

**Key words:** Geriatric Nutritional Risk Index (GNRI), total lymphocytes count, immune system, long-term care, elderly

**Objective:** To investigate how total lymphocyte count (TLC) and the Geriatric Nutritional Risk Index (GNRI) are associated with short-term nutritional-related complications (death, infections, bedsores) in institutionalised elderly.

**Methods:** 220 home-care resident elderly (age  $\pm$  SD;  $80.7 \pm 7.9$ , range: 67–98 years) were studied (anthropometry, biochemistry, food intake) and prospectively followed over a period of 3 months for the occurrence of health complications. Nutritional risk was assessed by GNRI. Patients were categorized according to GNRI (<92, 92–98, >98) and TLC (<900, 900–1499,  $\geq 1500/\text{mm}^3$ ).

**Results:** GNRI was significantly associated with TLC according to both simple and adjusted correlation models ( $p < 0.001$ ) and to multiple stepwise regression analysis ( $p < 0.005$ ). TLC < 900 revealed a higher specificity (87.8%) than sensitivity (30.6%) in identifying “at-risk” patients (GNRI < 92). Adjusted multiple logistic regression revealed a significant association between overall 3-month health outcomes and both TLC and food intake. TLC was the only significant predictor for infections, while death was independently associated with GNRI and food intake. When a GNRI < 92 and a TLC < 900 were considered together, the sensitivity was 0.83 (95% confidence interval, C.I.95%: 0.66–1.0) and 0.89 (C.I.95%: 0.68–1.00) for overall complications (Odds ratio: 22.1; C.I.95%: 5.1–96.1) and infections (Odds ratio: 20.8; C.I.95%: 2.6–168.8), respectively. The association of a GNRI > 98 with a TLC  $\geq 1500$  was able to exclude health complications.

**Conclusions:** In the institutionalised elderly patients, GNRI confirmed its predictive value even for short-term health complications, particularly when death was considered. However, the use of TLC might improve the evaluation of nutritional risk and the identification of patients at risk of infections. Nutrition study should be considered to confirm possible risk reduction

## INTRODUCTION

Malnutrition is a widespread problem in the elderly [1–4] and has been singled out as the most common cause of secondary immunologic dysfunction [2,5,6]. Older individuals frequently experience difficulties in eating and swallowing and nutrition deficiencies often occur. In turn, poor nutrient intakes

may result in a reduction of lymphocyte count and above all in functional alterations of both cellular and humoral response [7,8]. Nutrient supplementation is often accompanied by an improvement in immune function, although the lack of response (e.g. replication of lymphocytes) to refeeding has been invoked in explaining why the elderly are prone to infections [9]. Moreover, immune function has also been regarded among

---

Address correspondence to: Dr. Emanuele Cereda, International Center for the Assessment of Nutritional Status (ICANS), University of Milan, via Botticelli 21, 20133 Milan, Italy. E-mail: emanuele.cereda@virgilio.it

The Authors certify that there are no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript.

Dr. Cereda is currently affiliated to International Center for the Assessment of Nutritional Status (ICANS), whose director is Professor Giulio Testolin.

Abbreviations: GNRI = Geriatric Nutritional Risk Index, TLC = total lymphocytes count, AMA = arm muscle area

those factors contributing to compromised wound healing in presence of poor nutrition status [10–12].

There is some controversy about considering total lymphocytes count (TLC) as a suitable marker of protein-calorie malnutrition in the elderly, in fact some studies have described a decrease of TLC with progressive malnutrition [2,5,6,11], while others have reported a lack of correlation with nutritional status [13,14]. However, TLC has been considered a useful indicator of outcome [15,16] although little is known about its role and weight in the development of the patient's global nutritional risk.

Nowadays, it is well accepted that early screening and treatment of patients at risk of malnutrition provide the opportunity to start treatment at an early stage of hospitalisation so reducing the length of hospital stay, costs and the risks of morbidity and mortality [17]. To this purpose, a new scoring system to describe the nutritional-related risk of health complications (mortality, infections or bedsores) has recently been proposed and investigated: the Geriatric Nutritional Risk Index (GNRI) [4,18–20]. GNRI categories are defined on the basis of albumin concentrations and degrees of weight loss [4], while no attention has been paid to immunocompetence in the evaluation of outcomes. On the other hand, mortality, infections and bedsores appear to be significantly associated with immune function [7,8,10–12,15,16]. In addition, death frequently represents the end-point of infectious diseases in aged people [4,21].

The present paper aims to investigate the relationship between GNRI and TLC and to analyse the implication of these parameters in affecting the outcome of an institutionalised geriatric population.

## **MATERIALS AND METHODS**

### **Subjects and Assessments**

The data analysed in the present study belongs to a larger observational study which aimed to evaluate the prevalence of malnutrition among hospitalised and institutionalised patients in Italy (PIMAI study - Project Iatrogenic Malnutrition in Italy). The present study was carried out according to the guidelines of the Declaration of Helsinki (1996) and written informed consent was obtained from every patient before all measurements and samplings were made. The analysis included 220 elderly (85 males, 135 females; BMI  $\pm$  SD:  $25.4 \pm 5.2$ , range: 14.2–39.2 Kg/m<sup>2</sup>; age  $\pm$  SD:  $80.7 \pm 7.9$ , range: 67–98 years) living in two different long-term care structures of the province of Como. Baseline data collecting was performed over a 2-month period (February–March 2005). Exclusion criteria were: neoplastic disorders, renal or liver pathologies and use of medications affecting TLC (corticosteroids, cyclosporine or other main immunosuppressive drugs). All the subjects were assessed for anthropometric variables. Weight was measured to

the nearest 0.1 Kg by the same calibrated scale. A chair scale or hoist provided weighting device were used for those non-ambulatory and bedridden, respectively. Mid-upper arm circumference was measured by a flexible tape (to the nearest 0.5 cm) and triceps skinfold (to the nearest 0.2 mm) by a Holtain calliper. Finally, knee-height (to the nearest 0.5 cm) was assessed by an anthropometric calliper, according to standard procedures previously described [22] and estimated height was obtained using the specific equation of Chumlea et al. [23]. Body mass index (BMI) was defined as weight in kilograms divided by height in meters squared (Kg/m<sup>2</sup>) and arm muscle area (AMA) was calculated according to the validated formula [24]. The weight loss from the previous three months was obtained from the clinical register of every patient and its percentage was accordingly calculated. Baseline nutritional intake was assessed as follows. The amounts of food delivered to and left by the patients at the end of three main meals (breakfast, lunch, dinner) were weighted and recorded by the same well-trained dietitian. Oral intake was calculated as the percentage of food consumed and the mean of three consecutive days was considered for statistical analyses. 8 to 12 hours-fasting venous blood samples were assessed for baseline albumin, pre-albumin, transferrin and TLC according to standard laboratory procedures.

### **Nutritional Risk Scoring**

Patients were scored according to GNRI [GNRI = (1.489  $\times$  albumin, g/L) + (41.7  $\times$  weight/ideal body weight)] and categorized as follows: severe/moderate risk, <92; low risk, 92 to 98; no risk, >98 [4]. Subjects were also divided into three groups according to TLC (very low, <900; low-normal, 900–1499; normal,  $\geq 1500/\text{mm}^3$ ) as decrease in TLC to less than 900/mm<sup>3</sup> reflects severe malnutrition [2,13,25] and significant increase in mortality has been reported with a TLC of less than 1500/mm<sup>3</sup> [2,25,26]. No separation was adopted to discriminate “severe risk” (GNRI, <82) and “moderate risk” group (GNRI: 82 to <92) because these two categories have been demonstrated to present a similar increased risk (odds ratio) of health complications other than mortality (bedsores or infections) [4]. Moreover this categorization gave a three-category division similar to TLC.

### **Follow-Up and Outcomes**

The patients were followed for 3 months (up to the end of June 2005). At the end of this time window major complications were collected from the clinical register of every patient: infections (septicemia, pneumonia, urinary tract infection, candida), bedsores and death. Sepsis was defined as: fever (>38 °C) or hypothermia (<36 °C) and  $\geq 1$  positive blood culture for pathogenic organisms; pneumonia was diagnosed in presence of fever (>38 °C), a clinical sign, and radiographic confirmation; urinary tract infection required fever (>38 °C), a clinical sign, and bacteriologic confirmation of  $\geq 10^5$  organisms/mL

urine; candida infection required the isolation of *Candida spp* on secretion (oral, genital, cutaneous) by tampon sampling. When infections and bedsores were diagnosed, antibiotic therapy and medications were provided according to standard protocols.

## Statistics

Simple correlations (Pearson's correlation model) were assessed between baseline variables. Differences between the groups were investigated using the analysis of variance (ANOVA) and control for overall type 1 error was performed by Scheffe's post-hoc comparison test. Stepwise regression analysis was performed in order to assess the association of prognostic parameters with nutritional risk (GNRI).

A high sensitivity is required for a good screening tool. Thus, a  $TLC < 900/mm^3$  was investigated for sensitivity, specificity and predictive values (positive and negative) in identifying patients "at nutritional risk" ( $GNRI < 92$ ).

Sex and age-adjusted univariate logistic regression was performed to identify the continuous variables associated with overall health complications. Then, the correlates were analysed by multivariate model in order to evaluate independent associations with overall and single outcomes and the corresponding odds ratios (ORs) and 95% confidence intervals (C.I.95%) by each 1-SD increase in variables calculated. Moreover, focusing on the association between TLC and GNRI in determining complications, multivariate regressions were carried out also adding the interaction term  $TLC \times GNRI$ .

The sensitivity of different GNRI and TLC cut-offs was calculated in order to evaluate the reliability of these tools in predicting overall and single-taken nutritional complications. Finally, OR and C.I.95% were calculated to determine risk complications in high risk patients ( $GNRI < 92$  and  $TLC < 900$ ).

All statistical analysis were performed by STATISTIX 7.0 (Analytical Software, Tallahassee, FL, USA). Level of significance was set to a p value  $< 0.05$ .

## RESULTS

Clinical, anthropometric and biochemical characteristics of the GNRI and TLC categories are presented in Table 1. As previously described on a similar series, a high level of association was detected between the GNRI score and most of the parameters investigated [18], with the exception of AMA and age. However, with regard to TLC, the only powerful associations and differences were found for weight loss, albumin and GNRI (Fig. 1). A mild association was additionally detected with pre-albumin and mean oral intake.

It is noteworthy that the association between GNRI and TLC remained significant even after correcting for age, sex, BMI, oral intake and weight loss ( $r = 0.22$ ). In order to better

investigate the role of prognostic factors in risk development (GNRI), a stepwise regression analysis was conducted including the following variables: age, sex, BMI, weight loss, TLC and oral intake. GNRI most closely correlated with oral intake ( $p < 0.0001$ ) and to a lesser extent with BMI and TLC ( $p < 0.01$  and  $p < 0.005$ , respectively), while the other variables did not enter the model.

Referring to GNRI and TLC cut-offs (severe-moderate risk,  $GNRI < 92$ ,  $TLC < 900$ ; low risk,  $GNRI: 92$  to  $98$ ,  $TLC: 900$  to  $1499$ ; no risk,  $GNRI > 98$ ,  $TLC \geq 1500$ ) patients were classified as follows: 22.2%, 35%, 42.8% for GNRI and 16.4%, 28.6%, 55% for TLC (Table 2). According to these categorisations, a low TLC ( $< 900/mm^3$ ) revealed a higher specificity (0.88; C.I.95%: 0.83–0.93) and negative predictive value (0.825; C.I.95%: 0.77–0.87) than sensitivity (0.31; C.I.95%: 0.18–0.44) and positive predictive value (0.42; C.I.95%: 0.26–0.58) in identifying high nutritional risk ( $GNRI < 92$ ).

After the 3-month follow-up period major complications occurred in 18 (8.2 %) patients: 9 (4.1 %) had infectious complications (5 pneumonia; 1 sepsis; 2 urinary tract infection; 1 candida), 3 (1.4%) developed bedsores (sacral) and 6 (2.7%) died (2, pneumonia; 1, sepsis; 1 stroke; 2 heart disease). Complicated patients showed significantly lower values of oral intake, albumin, pre-albumin, TLC and were at higher nutritional risk (Table 3). The already listed parameters also showed a significant association with overall health outcomes when included in sex and age-adjusted univariate logistic regressions such as independent variables: albumin,  $p < 0.005$  (OR: 0.21; C.I.95%: 0.08–0.58); pre-albumin,  $p < 0.005$  (OR: 0.88; C.I.95%: 0.80–0.96); GNRI,  $p < 0.005$  (OR: 0.92; C.I.95%: 0.87–0.97); oral intake,  $p < 0.0005$  (OR: 0.95; C.I.95%: 0.93–0.98); TLC,  $p < 0.005$  (OR: 0.86; C.I.95%: 0.78–0.95). Therefore, multivariate models (Table 4) were carried out to evaluate independent association with overall and single complications. Albumin was excluded from the analyses because GNRI formula was structured to give high weight to this parameter [4] and its inclusion might have given distorted results. TLC and oral intake were significantly linked to overall health complications. However, with regard to a single complication, TLC was the only significant predictor for infections, while death was independently associated with GNRI and oral intake. No variable was found associated with bedsores. Finally, when performing an additional set of analyses, no significant association was detected for the interaction term  $TLC \times GNRI$ .

For overall complications, the sensitivity of GNRI and TLC cut-offs were as follows:  $GNRI < 92 = 0.56$  (C.I.95%: 0.33–0.79);  $GNRI \leq 98 = 0.94$  (C.I.95%: 0.86–1.0);  $TLC < 900 = 0.44$  (C.I.95%: 0.21–0.67);  $TLC < 1500 = 0.61$  (C.I.95%: 0.39–0.83). However, with regard to single complications, a GNRI score  $< 92$  showed the best sensitivity (100%) in death prediction, in spite of a poor capacity in identifying those at risk of infectious complications (0.33; C.I.95%: 0.03–0.63). Conversely, TLC showed a higher prediction for infections ( $TLC < 900: 0.78$ , C.I.95%: 0.74–

**Table 1.** Statistical Comparison of Nutritional (Anthropometric and Biochemical) Variables among GNRI and TLC Categories

	Geriatric Nutritional Risk Index			One-way ANOVA	Pearson's Coefficient	Total Lymphocytes Count (/mm <sup>3</sup> )			One-way ANOVA	Pearson's Coefficient
	High <92	Medium 92-98	No risk >98			Very low <900	Low-normal 900-1499	Normal ≥1500		
	n	n	n			n	n	n		
Age (years)	49	77	94	>0.05	-0.15§	36	63	121	>0.05	0.08
BMI (Kg/m <sup>2</sup> )	82.8 ± 7.0	80.1 ± 7.5	80.1 ± 8.5	<0.0001*	0.37**	80.1 ± 7.3	80.6 ± 7.7	80.9 ± 8.2	>0.05	0.09
MUAC (cm)	21.9 ± 4.7	26.0 ± 5.5	26.7 ± 4.2	<0.0001*	0.30**	25.0 ± 5.3	24.5 ± 5.0	25.9 ± 5.2	>0.05	-0.01
TSF (mm)	24.3 ± 4.5	28.3 ± 4.7	28.3 ± 4.2	<0.0005*	0.23‡	28.0 ± 4.8	26.7 ± 4.7	27.6 ± 4.7	>0.05	0.05
AMA (cm <sup>2</sup> )	11.5 ± 5.6	15.9 ± 7.6	16.2 ± 6.9	<0.0005*	0.15§	15.0 ± 7.7	14.3 ± 6.3	15.4 ± 7.4	>0.05	-0.08
Weight Loss (%)	42.6 ± 21.2	56.9 ± 25.7	53.9 ± 23.7	<0.0001*	0.47**	58.6 ± 25.5	51.7 ± 23.9	51.0 ± 24.2	<0.0005*	0.15§
Oral Intake (%)	-3.3 ± 4.7	-0.7 ± 3.3	-0.9 ± 2.5	<0.0001¶	0.90**	-3.2 ± 5.1	-1.3 ± 3.2	-0.9 ± 3.0	<0.0001*	0.22†
Albumin (g/L)	59.5 ± 22.1	78.1 ± 17.0	82.7 ± 14.7	<0.0001¶	0.46**	67.1 ± 20.1	76.3 ± 13.6	79.0 ± 19.2	<0.0001*	0.15§
Prealbumin (mg/dL)	32.0 ± 4.2	36.6 ± 2.3	41.1 ± 2.2	<0.0001¶	0.46**	34.7 ± 4.7	37.4 ± 4.4	38.3 ± 4.2	<0.0001*	0.23●
Transferrin (mg/dL)	14.7 ± 6.9	20.8 ± 5.9	23.1 ± 6.1	<0.0001*	0.46**	15.9 ± 5.9	20.9 ± 6.4	21.4 ± 6.9	<0.0005*	0.16§
TLC (/mm <sup>3</sup> )	175.4 ± 40.3	189.5 ± 28.8	210.9 ± 35.1	<0.0001*	0.46**	220.2 ± 53.8	200.9 ± 33.7	195.4 ± 36.5	>0.05	0.02
GNRI	1335 ± 571	1663 ± 799	1858 ± 672	<0.0005¶	0.23●	686 ± 188.1	1234 ± 155	2164 ± 552	<0.0001¶	-
	85.4 ± 5.9	94.9 ± 1.8	102.5 ± 3.3	<0.0001¶	-	91.8 ± 7.1	95.4 ± 8.2	97.6 ± 6.9	<0.0005*	0.23●

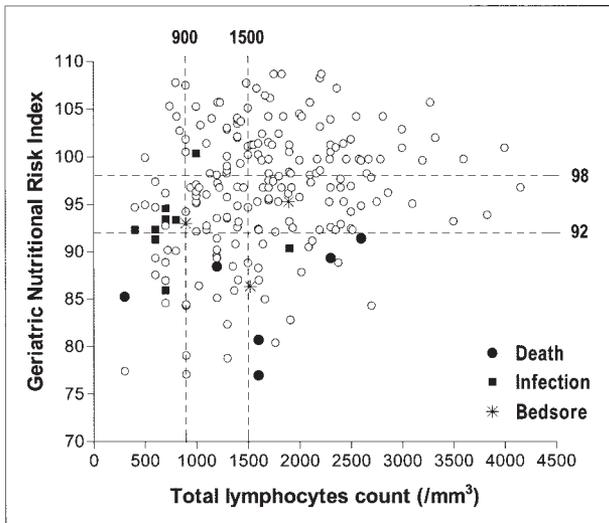
Data are expressed as mean ± SD, BMI = body mass index, MUAC = mid-upper arm circumference, TSF = triceps skinfold, AMA = arm muscle area, TLC = total lymphocytes count, GNRI = Geriatric Nutritional Risk Index.

Quantitative variables were compared by ANOVA analysis.

Post-hoc comparison of means was performed by Scheffe's test.

¶ all group significantly different from one another; \*groups GNRI < 92 and TLC < 900 significantly different from the other categories.

§ Significance values for Pearson's correlation model: §p < 0.05; †p < 0.005; ‡p < 0.001; ●p < 0.0005; \*\*p < 0.0001.



**Fig. 1.** Correlation between Geriatric Nutritional Risk Index (score) and total lymphocytes count according to Pearson’s simple correlation model ( $r = 0.23$ ;  $p < 0.0005$ ) and their association with 3-month outcome.

0.82;  $TLC < 1500 = 0.89$ , C.I.95%: 0.68–1.00) rather than for death ( $TLC < 900 = 0.17$ , C.I.95%: 0.00–0.46;  $TLC < 1500 = 0.33$ , C.I.95%: 0.00–0.38). When a GNRI  $< 92$  and a  $TLC < 900$  were considered together, the sensitivity was 0.83 (C.I.95%: 0.66–1.0) and 0.89 (C.I.95%: 0.68–1.00) for overall complications and infections, respectively. The risk (OR) of overall outcomes and infections of the population identified by these cut-offs ( $n = 70$ ), compared to that of the other patients ( $n = 150$ ; OR = 1), were 22.1 (C.I.95%: 5.1–96.1) and 20.8 (C.I.95%: 2.6–168.8) respectively.

The association of a GNRI  $> 98$  with a  $TLC \geq 1500$  seemed to exclude the occurring of complications with high reliability (Fig. 1).

## DISCUSSION

Previous report have suggested that aging may contribute to TLC reduction, particularly by decreasing inducible lymphocyte

proliferation and declining thymulin activity [2,7–9,13,15]. However, this participation does not seem to be supported by our findings.

In the present study, a significant interrelationship was found between a group of well known prognostic factors [2,27–29], such as GNRI, TLC, albumin oral intake and percentage of weight loss. Moreover, TLC seems to significantly contribute to total geriatric nutritional risk, as suggested by both unadjusted and adjusted models as well as by stepwise regression analysis. Malnutrition may be the mirror of a stress-related inflammatory background frequently leading to hypoxemia, weight loss and immune dysfunction [6,30,31]. GNRI has been structured to take into account the acute complications, through albumin, and the availability of protein-calorie stores to face them, through the body weight factors. This last element may also reflect a history of acute or chronic undernutrition and weight loss.

It is not clear if TLC reduction is a consequence of an acute stress or sides a progressive depletion of body stores. It has been speculated that morbid process might trigger a stress-related increase of steroid levels that could lead to lymphopenia [2,7–9,32] and our findings on the correlation between TLC, GNRI, albumin and weight loss seem to support this hypothesis. We may suppose that as long as an acute stress acts in presence of reduced energy stores, or stores depletion, a progressive lowering of TLC may occur after an initial functional impairment [9,32]. In fact, a low BMI or an important involuntary weight loss are associated with increased susceptibility to infections and their effects on lymphocytes seem to be a common denominator [2,11,33]. In our study, no association was found between weight loss and the occurrence of overall complications, but we can not exclude that weight reduction could be occurred after baseline evaluations. This could also explain the higher prognostic value of oral intake and TLC. In the past, attention was paid not only to TLC but also, and particularly, to the lymphocytes function (e.g. cytokine release, proliferation or delayed hypersensitivity) whose impairment have already been demonstrated both with the occurring of protein-calorie malnutrition and the impairment of several nutrients (protein, iron and zinc) [2,7,8,12,32–35]. Accordingly, an improvement of cell-mediated immune function has been

**Table 2.** Comparison of Geriatric Nutritional Risk Index (GNRI) and Total Lymphocytes Count in the Assessment of Both Nutritional Risk and Health Complications (Death, Infections, Bedsore)

	Total Lymphocytes Count (/mm <sup>3</sup> )			Total
	Very low $< 900$	Low-normal 900–1499	Normal $\geq 1500$	
Risk by GNRI				
High: $< 92$	15 (6.8) [1;2;0]	17 (7.7) [1;0;0]	17 (7.7) [4;1;1]	49 (22.2) [6;3;1]
Medium: 92 to 98	13 (5.9) [0;5;0]	22 (10) [0;0;1]	42 (19.1) [0;0;1]	77 (35) [0;5;2]
No risk: $> 98$	8 (3.7) [0;0;0]	24 (10.9) [0;1;0]	62 (28.2) [0;0;0]	94 (42.8) [0;1;0]
Total	36 (16.4) [1;7;0]	63 (28.6) [1;1;1]	121 (55) [4;1;2]	220 (100) [6;9;3]

Prevalence are presented as  $n$  and % (between parentheses); count of health complications are provided between square brackets [death; infections; bedsore].

**Table 3.** Characteristic of the Complicated Patients Compared to those Complication-Free

	Complicated (n = 18)	Uncomplicated (n = 202)	P-value
Age (years)	82.9 ± 6.4	80.4 ± 7.8	>0.05
BMI (Kg/m <sup>2</sup> )	24.8 ± 5.6	25.3 ± 5.2	>0.05
MUAC (cm)	27.8 ± 5.0	27.2 ± 4.8	>0.05
TSF (mm)	15.4 ± 9.0	14.6 ± 6.6	>0.05
AMA (cm <sup>2</sup> )	58.8 ± 23.7	50.9 ± 24.4	>0.05
Weight Loss (%)	-3.2 ± 3.6	-1.8 ± 3.7	>0.05
Oral Intake (%)	56.4 ± 21.6	76.7 ± 18.6	<0.0001
Albumin (g/L)	33.7 ± 3.2	37.5 ± 4.6	0.0001
Prealbumin (mg/dL)	14.9 ± 5.9	20.6 ± 6.8	0.0024
Transferrin (mg/dL)	170.5 ± 41.7	197.3 ± 38.3	>0.05
TLC (/mm <sup>3</sup> )	1173 ± 691	1687 ± 694	0.0032
GNRI	89.8 ± 6.5	96.0 ± 7.7	0.0011

Complications were: infections (n = 9), bedsores (n = 3) and death (n = 6). Comparison between groups was performed by two-sample t-test; P-values were chosen according to test for equal-unequal variances.

**Table 4.** Sex and Age-Adjusted Odds Ratios of Health Complications per SD Increase in Variables according to Multivariate Logistic Regression Model

	Beta coefficient	Std. error	P-value	OR [95% C.I.]
Overall				
GNRI	-0.00683	0.04759	0.8859	0.99 [0.90-1.09]
Oral intake	-0.03821	0.01566	0.0147	0.96 [0.93-0.99]
TLC	-0.09737	0.04892	0.0465	0.91 [0.82-1.00]
Pre-albumin	-0.06375	0.05098	0.2112	0.94 [0.85-1.04]
Infection				
GNRI	0.10286	0.07604	0.1761	1.11 [0.95-1.29]
Oral intake	-0.01801	0.02174	0.4074	0.98 [0.94-1.02]
TLC	-0.24531	0.09604	0.0106	0.78 [0.65-0.94]
Pre-albumin	-0.16150	0.09238	0.0804	0.85 [0.71-1.02]
Bed sore				
GNRI	0.02345	0.12435	0.8505	1.02 [0.80-1.31]
Oral intake	-0.02130	0.02793	0.4456	0.98 [0.93-1.03]
TLC	-0.01415	0.08170	0.8625	0.99 [0.84-1.16]
Pre-albumin	-0.21796	0.15023	0.1468	0.80 [0.60-1.08]
Death				
GNRI	-0.19828	0.09523	0.0373	0.82 [0.68-0.99]
Oral intake	-0.06640	0.02998	0.0268	0.94 [0.88-0.99]
TLC	0.10736	0.08368	0.1995	1.11 [0.94-1.31]
Pre-albumin	0.13423	0.08159	0.0999	1.14 [0.97-1.34]

SD = standard deviation, GNRI = Geriatric Nutritional Risk Index, TLC = Total Lymphocytes Count, Std. error = standard error, OR = Odds Ratio, [95% C.I.] = 95% Confidence Interval.

Levels (mean ± SD) for the variables in the population were: GNRI score: 95.4 ± 7.8, Oral intake: 74.8 ± 19.8%, TLC: 16.4 ± 7.1 × 10<sup>3</sup>/mm<sup>3</sup>, Pre-albumin: 20 ± 6.9 mg/dL.

demonstrated in both human and animal-model studies when nutritional repletion [5], micronutrients supplementation [36, 37] or immune-enhancing diet administration are provided [38]. Though, the restoration of immunocompetence appears compromised in the elderly [9]. In our analysis, lymphocyte function, as well as the distinction of different T lymphocytes' subpopulations and the role of micronutrients, were not taken into account due to data unavailability and future investigations should be made in this direction. However, the possible effect of reduced nutritional intake was partly investigated, and its role in affecting both TLC and nutritional risk might be suggested [29]. This fact has important consequences in

the assessment of the institutionalised patient, particularly when considering the frequent difficulties experienced in both eating and swallowing and the high prevalence of malnutrition in long-term care [39].

GNRI was designed and validated in a geriatric rehabilitative setting according to a 6-months severity score and no more longitudinal analyses have been performed to assess its short-term reliability in different settings. The only exception is represented by a previous evaluation of short-term mortality prediction in acutely hospitalised elderly [19]. The present results show that GNRI alone confirms its predictive value [4,19] when short-term complications occur, even in a

long-term care setting, particularly when death is considered. However, when a “low risk” is scored (GNRI: 92 to 98) by adding TLC ( $<900/\text{mm}^3$ ) there is an improvement in the infection risk assessment, thus signifying the need for nutritional intervention.

As a high sensitivity is required for screening procedures and in order to apply preventive strategies, both GNRI and TLC should be used together in routine assessments.

In agreement with previous observations, TLC should not be considered a screening tool for nutritional status [13]. Moreover, TLC per-se should not be considered a reliable predictor of overall short-term nutritional complications, particularly of death, which is in contrast with previous report describing a significant increase in mortality among those acutely hospitalised and presenting a TLC  $< 1500 \text{ mm}^3$  [26]. Perhaps, the different setting of our study (long-term care) and the patient profile (not acute) could explain this. Alternatively, TLC could help in the prediction of infectious complications and an almost normal value ( $\geq 1500/\text{mm}^3$ ) would seem to represent a margin of safety.

The routine use of TLC might improve the evaluation of nutritional risk but this suggestion deserves confirmation. Further prospective analyses should be made to quantify the role of TLC and immune function together with other well known prognostic factors. Moreover, nutrition studies should be considered to confirm possible risk reduction.

## CONCLUSION

A large proportion of the elderly have reduced dietary intakes, resulting in malnutrition or risk of malnutrition and immunologic dysfunction. Different screening tools, such as the new Geriatric Nutritional Risk Index, have been proposed to reliably identify those at risk of health complications (death, infections, bedsores) and to guide nutritional intervention. However, some easy and readily available measures, such as peripheral blood lymphocyte count, could still provide useful information on the patient’s risk, particularly for infectious complications. Simple indicators should be taken into greater consideration.

## ACKNOWLEDGEMENTS

We gratefully acknowledge Prof. Alberto Battezzati and Dr. Simona Bertoli for their assistance in drafting the manuscript.

## REFERENCES

1. Omran ML, Morley JE: Assessment of protein energy malnutrition in older persons, part I: History, examination, body composition, and screening tools. *Nutrition* 16:50–63, 2000.

2. Omran ML, Morley JE: Assessment of protein energy malnutrition in older persons, Part II: Laboratory evaluation. *Nutrition* 16:131–140, 2000.
3. Persson MD, Brismar KE, Katzarski KS, Nordenstrom J, Cederholm TE: Nutritional status using mini nutritional assessment and subjective global assessment predict mortality in geriatric patients. *J Am Geriatr Soc* 50:1996–2002, 2002.
4. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, Benazeth S, Cynober L, Aussel C: Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr* 82:777–783, 2005.
5. Law DK, Dudrik SJ, Abdou NI: Immunocompetence of patients with protein-calorie malnutrition. The effect of nutritional repletion. *Ann Intern Med* 79:545–550, 1973.
6. Bistran BR, Blackburn GL, Scrimshaw NS, Flatt JP: Cellular immunity in semistarved states in hospitalized adults. *Am J Clin Nutr* 28:1148–55, 1975.
7. Chandra RK: Nutrition and the immune system from birth to old age. *Eur J Clin Nutr* 56(Suppl 3):S73–76, 2002.
8. Ahluwalia N: Aging, nutrition and immune function. *J Nutr Health Aging* 8:2–6, 2004.
9. Walrand S, Moreau K, Caldefie F, Tridon A, Chassagne J, Portefaix G, Cynober L, Beaufre B, Vasson MP, Boirie Y: Specific and nonspecific immune responses to fasting and refeeding differ in healthy young adult and elderly persons. *Am J Clin Nutr* 74:670–678, 2001.
10. Thomas DR: Improving outcome of pressure ulcers with nutritional interventions: a review of the evidence. *Nutrition* 17:121–125, 2001.
11. Allman RM, Goode PS, Patrick MM, Burst N, Bartolucci AA: Pressure ulcer risk factors among hospitalized patients with activity limitation. *JAMA* 273:865–870, 1995.
12. Hudgens J, Langkamp-Henken B, Stechmiller JK, Herrlinger-Garcia KA, Nieves C Jr: Immune function is impaired with a mini nutritional assessment score indicative of malnutrition in nursing home elders with pressure ulcers. *J Parenter Enteral Nutr* 28:416–422, 2004.
13. Kuzuya M, Kanda S, Koike T, Suzuki Y, Iguchi A: Lack of correlation between total lymphocyte count and nutritional status in the elderly. *Clin Nutr* 24:427–432, 2005.
14. Ruiz-Lopez MD, Artacho R, Oliva P, Moreno-Torres R, Bolanos J, de Teresa C, Lopez MC: Nutritional risk in institutionalized older women determined by the Mini Nutritional Assessment test: what are the main factors? *Nutrition* 19:767–771, 2003.
15. Izaks GJ, Remarque EJ, Becker SV, Westendorp RG: Lymphocyte count and mortality risk in older persons. The Leiden 85-Plus Study. *J Am Geriatr Soc* 51:1461–1465, 2003.
16. Bender BS, Nagel JE, Adler WH, Andres R: Absolute peripheral blood lymphocyte count and subsequent mortality of elder men (The Baltimore Longitudinal Study of Aging). *J Am Geriatr Soc* 34:649–654, 1986.
17. Kruizenga HM, Van Tulder MW, Seidell JC, Thijs A, Ader HJ, Van Bokhorst-de van der Schueren MA: Effectiveness and cost-effectiveness of early screening and treatment of malnourished patients. *Am J Clin Nutr* 82:1082–1089, 2005.
18. Cereda E, Limonta D, Pusani C, Vanotti A: Assessing elderly at risk of malnutrition: the new Geriatric Nutritional Risk Index versus Nutritional Risk Index. *Nutrition* 22:680–682, 2006.

19. Cereda E, Limonta D, Pusani C, Vanotti A: Geriatric nutritional risk index: a possible indicator of short-term mortality in acutely hospitalized older people. *J Am Geriatr Soc* 54:1011–1012, 2006.
20. Cereda E, Vanotti A: The new Geriatric Nutritional Risk Index is a good predictor of muscle dysfunction in institutionalized older patients. *Clin Nutr* 26:78–83, 2007.
21. Tacconelli E, Pop-Vicas AE, D'Agata EM: Increased mortality among elderly patients with methicillin-resistant *Staphylococcus aureus* bacteraemia. *J Hosp Infect* 64:251–256, 2006.
22. Cereda E, Limonta D, Pusani C, Vanotti A: Feasible use of estimated height for predicting outcome by the Geriatric Nutritional Risk Index in long-term care resident elderly. *Gerontology* 53:184–186, 2007.
23. Chumlea WC, Roche AF, Steinbaugh ML: Estimating stature from knee height for persons 60 to 90 years of age. *J Am Geriatr Soc* 33:116–120, 1985.
24. Frischno AR: New norms of upper limb fat and muscle areas for assessment of nutritional status. *Am J Clin Nutr* 34:2540–2555, 1981.
25. Seiler WO: Clinical pictures of malnutrition in ill elderly subjects. *Nutrition* 17:496–498, 2001.
26. Seltzer MH, Bastidas JA, Cooper DM, Engler P, Slocum B, Fletcher HS: Instant nutritional assessment. *JPEN J Parenter Enteral Nutr* 3:157–159, 1979.
27. Beck AM, Ovesen L: At which body mass index and degree of weight loss should hospitalized elderly patients be considered at nutritional risk? *Clin Nutr* 17:195–198, 1998.
28. Klonoff-Cohen H, Barrett-Connor EL, Edelstein SL: Albumin levels as a predictor of mortality in the healthy elderly. *J Clin Epidemiol* 45:207–212, 1992.
29. Kagansky N, Berner Y, Koren-Morag N, Perelman L, Knobler H, Levy S: Poor nutritional habits are predictors of poor outcome in very old hospitalised patients. *Am J Clin Nutr* 82:784–791, 2005.
30. Morley JE, Thomas DR, Wilson MM: Cachexia: pathophysiology and clinical relevance. *Am J Clin Nutr* 83:735–743, 2006.
31. Stratton RJ, King CL, Stroud MA, Jackson AA, Elia M: 'Malnutrition Universal Screening Tool' predicts mortality and length of hospital stay in acutely ill elderly. *Br J Nutr* 95:325–330, 2006.
32. Stephensen CB: Examining the effect of a nutrition intervention on immune function in healthy humans: what do we mean by immune function and who is really healthy anyway? *Am J Clin Nutr* 74:565–566, 2001.
33. Buzby GP, Knox LS, Crosby LO, Eisenberg JM, Haakenson CM, McNeal GE, Page CP, Peterson OL, Reinhardt GF, Williford WO: Study protocol: a randomised clinical trial of total parenteral nutrition in malnourished surgical patients. *Am J Clin Nutr* 47(Suppl):366–381, 1988.
34. Finamore A, Devirgiliis C, Panno D, D'Aquino M, Polito A, Venneria E, Raguzzini A, Coudray C, Mengheri E: Immune response in relation to zinc status, sex and antioxidant defence in Italian elderly population: the ZENITH study. *Eur J Clin Nutr* 59(Suppl 2):S68–72, 2005.
35. Dardenne M: Zinc and immune function. *Eur J Clin Nutr* 56 (Suppl 3):S20–23, 2002.
36. Peretz A, Neve J, Desmedt J, Duchateau J, Dramaix M, Famaey JP: Lymphocyte response is enhanced by supplementation of elderly subjects with selenium-enriched yeast. *Am J Clin Nutr* 53:1323–1328, 1991.
37. Ravaglia G, Forti P, Maioli F, Bastagli L, Facchini A, Mariani E, Savarino L, Sassi S, Cucinotta D, Lenaz G: Effect of micronutrient status on natural killer cell immune function in healthy free-living subjects aged  $\geq 90$  y. *Am J Clin Nutr* 71:590–598, 2000.
38. Belabed L, Charrueau C, Besson V, Gupta S, Walrand S, Marchand-Verrecchia C, Richon S, Nafziger J, Plotkine M, Chaumeil JC, Cynober L, Moinard C: Impairment of lymphocyte function in head-injured rats: effects of standard and immune-enhancing diets for enteral nutrition. *Clin Nutr* 25:832–841, 2006.
39. Thomas DR, Ashmen W, Morley JE, Evans WJ: Nutritional management in long-term care: development of a clinical guideline. Council for Nutritional Strategies in Long-Term Care. *J Gerontol A Biol Sci Med Sci* 55:M725–734, 2000.

*Received February 15, 2007; revision accepted July 27, 2007.*