The use of biochemical and immunological parameters in nutritional screening and assessment

A. González Madroño¹, A. Mancha¹, F. J. Rodríguez², J. I. de Ulibarri¹ and J. Culebras³

¹Sección de Nutrición Clínica y Dietética. Hospital Universitario de La Princesa. ²Instituto de Investigación del Hospital Universitario de La Princesa. ³Servicio de Cirugía. Complejo Asistencial de la Universidad de León. Instituto de Biomedicina (IBIOMED). Universidad de León. España.

Abstract

Objective: To evaluate the relationship between serum albumin, total cholesterol and total lymphocyte count with two nutritional assessment methods, to verify if their use is justified in nutritional screening tools.

Methods: 101 patients admitted to medical/surgical wards underwent the SGA and the Full Nutritional Assessment (FNA). Blood test which included serum albumin, total cholesterol and total lymphocyte count (TLC), were made. Percentage of weight loss and BMI were calculated. An ANOVA test was done to measure the differences in the mean levels of the three parameters for the nutritional status evaluated by SGA and FNA. The probability of a patient being malnourished in the four ranges established for each parameter was calculated, as well as the relationship between the ranges and the percentage of weight loss and BMI. Sensitivity and specificity were calculated and the corresponding ROC curves, using SGA as gold standard.

Results: Prevalence of undernutrition is 43.6% and 44.6% for SGA and FNA respectively. Mean levels of the three parameters decrease as the undernutrition degree increases (p < 0.005 for all cases). The probability of a patient being malnourished gets higher as parameter lowers (p = 0.000 for all cases). Total cholesterol shows a relationship with BMI ≤ 18.5 and presence/absence of weight loss (p = 0.074 and p = 0.002 respectively). The area under ROC curves are albumin (0.823), cholesterol (0.790) and TLC (0.758) respectively.

Conclusions: The analytical parameters analyzed show a statistically significant relationship with the nutritional status. Therefore, they are suitable for use in nutritional screening.

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Correspondence: A. González Madroño.
Hospital Universitario de La Princesa.
Sección de Nutrición Clínica y Dietética.
C/Diego de León, 62.
28006 Madrid.
E-mail: ana_madrono@yahoo.com
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Introduction

For almost three decades, it has been recognized that hospital patients frequently present undernutrition or have a high probability of developing it due to their underlying disease and/or treatment received. The classic works, published in 1974 and 1976 by Bristian and col., reported that about 50% of patients admitted to a university hospital, in surgical and medical services, presented some degree of undernutrition varying from 45% to 54%.1,2

More recent studies continue to prove that the prevalence of undernutrition upon admission to hospital remains high, although the reported figures are quite variable and generally oscillate between 30% and 60%, depending on the diagnostic criteria employed and the specific population studied.3-5

Clinical undernutrition goes further than hospital undernutrition. It persists after discharge, extends length of stay and convalescence, increases sanitary costs and frequently leads to readmissions.10,16

There are many tools for nutritional screening and assessment. The most commonly used and widely validated are:

- Subjective Global Assessment (SGA) suggested by ASPEN for nutritional Assessment,17
- the Mini Nutritional Assessment (MNA) developed for elderly patients,18 Nutritional Risk Screening-2002 (NRS-2002),19 and the Malnutrition Universal Screening Tool (MUST) developed by the Malnutrition Advisory Group of BAPEN,20 all three recommended by the ESPEN to detect the prevalence of malnutrition.21 All of them are based on different clinical information such as body mass index (BMI), weight loss, intakes changes, eating difficulties, severity of disease, etc.

In an ideal situation personnel in charge of the patient assess the nutritional risk using one of these screening tools, and when malnourished patients are identified they are referred to the nutritional unit or team, and a nutritional intervention is decided. In practice this is difficult to carry out due to the lack of staff and consciousness of personal in charge of the patient so hospital undernutrition remains under diagnosed and therefore not treated.

In the past, analytical parameters were frequently used in nutritional indexes, combined with other nutritional status parameters, and they proved to be valid and reliable for this purpose. However, in the last years, analytical parameters have not been used for nutritional screening because many authors argue that they reflect severity of disease rather than nutritional status.22 Serum albumin and TLC are the most commonly used; the Nutritional Risk Index (NRI) is based on serum albumin and the ratio of actual to usual weight,23 the equation developed by Elmore includes serum albumin, TLC and % weight loss for nutritional screening,24 the Instant Nutritional Assessment (INA) combines both serum albumin and TLC for the screening.25

The aim of this study was to evaluate the relationship between serum albumin, total cholesterol and total lymphocyte count with different nutritional assessment methods and to verify if they are valid to be used in nutritional screening tools.

Methods

Subjects

The study was carried out in Hospital Universitario de la Princesa, a 500 beds hospital, only for adults, with approximately 17,000 patients admitted per year. Inclusion and exclusion criteria are as follows: 101 patients were randomly selected from all departments except from Psychiatric, Hemodialysis and Intensive Care Units. Patients with no routine analysis done during their first week of hospitalization, those who were admitted for a diagnostic test or a short term stay, or those who didn’t sign the inform consent were excluded from the study.
Assessments of nutritional state

Selected patients underwent two different nutritional assessments methods during their first week of hospitalization:

**Subjective Global Assessment (SGA)**, is made by a nutritionist of the Dietetic Unit. The SGA assesses nutritional status based on clinical history and physical examination. The history records data related to weight changes in the last six months, modification on diet intakes, presence of gastrointestinal symptoms and functional capacity. The physical examination includes: presence of loss of subcutaneous fat, muscle wasting, ankle oedema and ascites. The exam classifies patients as well nourished, moderately or suspected of being undernourished and severely malnourished.17

**Full Nutritional Assessment (FNA)**, is made by a physician of the Dietetic Unit. It is based on the SENPE (Sociedad Española de Nutrición Enteral y Parenteral) protocol for Nutritional Assessment. It includes:

- **Anamnesis**: principal diagnose, admission’s reason, food allergies and/or intolerances, metabolic disorders, presence of gastrointestinal symptoms, changes on diet intakes, digestive loss, personal records, previous surgeries, treatment.
- **Physical examination**: general look/aspect, loss of subcutaneous fat, muscle wasting, oedema, ascites, mucocutaneous lesions and changes in skin appendages.
- **Anthropometrics**: Patients were weighed, whenever clinically possible, using the scale available, they were asked about their height and an estimated weight six months prior to admission. Percentage of weight loss was calculated, as well as body mass index (BMI).
  
  This assessment classifies patients as well nourished, moderately or suspected of being malnourished and severely malnourished.

- **Blood test**: includes serum determinations of albumin, total cholesterol, total lymphocyte count, hemogram, pre-albumin, transferrin, iron, lipids profile, serum and urine ions (Na, K, Cl) and hepatic, renal and endocrine-metabolic function.

**Analytical variables and ranges**

The three parameters analyzed (serum albumin, total cholesterol and total lymphocyte count) are classified according to their normality or deficiency levels in four categories as shown in table I. Serum albumin (g/dL) is used as an indicator of protein reserves,26-28 total cholesterol (mg/dL) is used as a caloric depletion parameter,29-30 and finally, total lymphocyte (Cell/mL) count is used as an indicator of loss of immune defences caused by undernutrition.30-33 Serum albumin and total cholesterol were analyzed by a “Roche Modular Analyzer”, and total lymphocyte count was analyzed by a “Roche SYSMES Hematological”.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Light</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Albumin (g/dL)</td>
<td>3.5-4.5</td>
<td>3-3.49</td>
<td>2.5-2.9</td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>&gt; 180</td>
<td>140-180</td>
<td>100-139</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Total Lymphocyte Count/ml</td>
<td>&gt; 1,600</td>
<td>1,200-1,599</td>
<td>800-1,200</td>
<td>&lt; 800</td>
</tr>
</tbody>
</table>

**Table I**

Parameters classification according to their deficiency levels

**Statistical analysis**

Categorical variables were described as the number of cases and percentages and age with the mean ± standard deviation (SD). The association level between the results of the SGA and the FNA was measured using the \( \chi^2 \) Test, and the agreement degree was measured by contingency tables using the kappa index.34

The relationship between the three parameters and the nutritional status was measured as follows:

First, an ANOVA test was carried out to test the significance of the difference in the mean levels of albumin, cholesterol and lymphocytes for the three nutritional status evaluated by SGA and FNA.

Second, the probability of a patient being malnourished in the four ranges established for each parameter was calculated using contingency tables. For this analysis, patients were classified as malnourished (if moderately or severely undernourished) or not malnourished (if well nourished).

Third, the relationship between the three parameters and BMI and weight loss was tested by an ANOVA test. BMI was classified into two categories: BMI > or < than 18.5 as these ranges/limits are considered as an indicators of malnutrition, and weight loss was categorized in presence or absence.

Fourth, to compare the malnutrition diagnostic efficacy of the biochemical and immunological parameters studied, different efficacy rates were calculated (sensitivity, specificity, and their corresponding confidence intervals) for the different cut points and the corresponding ROC curves and Kruskall-Wallis tests). SGA was used as the gold standard.

The level of significance was established for a probability of 0.05. All tests were performed using SPSS package vs. 13.0.
Results

Subject

101 patients were studied, most of them hospitalized in medical wards (79.21%). Sample description is shown in table II. Of these patients 5 (4.9%) had no information about BMI, and 14 (13.9%) had none about weight loss. From those with data available, only 18.8% had a BMI lower than 20, and 53.4% had lost weight, and almost 18% had a weight loss greater than 10%.

Nutritional status evaluated by SGA and FNA is shown in table III. Note that the prevalence of undernutrition (moderate and severe) is close to 45% of the patients for both methods. SGA and FNA present a high concordance degree when evaluating undernutrition, as shown by kappa index = 0.787.

Mean levels of the three parameters for the nutritional status evaluated by SGA is shown in table IV. Notice that a decreased trend can be observed for the three of them as the undernutrition degree gets higher, and that this trend is statistically significant in all cases.

The probability of a patient being malnourished gets higher the lower the range for each parameter (table V), and this trend is statistically significant for the three parameters.

When analyzing the relationship of the parameters with BMI and weight loss (table VI), we can observe that some kind of relation exist for the three of them, so that the mean levels of albumin, cholesterol, and TLC are higher for individuals with a BMI > 18.5 or with no weight loss than for those with BMI < 18.5 and some weight loss, but these differences get significant levels only in the case of serum cholesterol.

Sensibility and specificity obtained for the three variables are shown in table VII.

Discussion

From the first studies published about the so called hospital undernutrition1-3 to the more recent ones,6-8 undernutrition prevalence rates have maintained a considerably high rate. There are multiple causes for that malnutrition, as the illness process itself, the hospitalization, the diagnostic and therapeutical procedures, which very often include fasting and the lack of interest about a patient’s nutritional status from the sanitary staff. Prevalence of malnutrition in our hospital is very high according to the SGA and FNA (43.6% and 44.6% respectively), and these results are consistent with other literature reports.35,36

Another reason for the continuation of these high undernutrition rates might be the lack of quick and cheap nutritional screening tools, applicable periodically to all inpatient populations, to alert about this serious sanitary issue. The aim of a nutritional screen-

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**Table II**

<table>
<thead>
<tr>
<th>Sample description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº of patients</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
</tr>
<tr>
<td>Males/Females, n (%)</td>
</tr>
<tr>
<td>Internal ward/Surgical ward n (%)</td>
</tr>
</tbody>
</table>

**BMI**

(n = 96), n (%)

- > 25: 53 (55.2)
- 20-25: 24 (25)
- 18.5-20: 9 (9.4)
- < 18.5: 10 (10.4)

**Percentage of weight loss**

(n = 87), n (%)

- No weight loss: 47 (54)
- < 5 %: 7 (8.1)
- 5-10 %: 15 (17.2)
- > 10 %: 18 (20.7)

BMI: Body Mass Index.

**Table III**

<table>
<thead>
<tr>
<th>FNA</th>
<th>Normal</th>
<th>Moderate UN</th>
<th>Severe UN</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA</td>
<td>53</td>
<td>4</td>
<td>0</td>
<td>57 (56.4)</td>
</tr>
<tr>
<td>Moderate UN</td>
<td>3</td>
<td>29</td>
<td>3</td>
<td>35 (34.7)</td>
</tr>
<tr>
<td>Severe UN</td>
<td>0</td>
<td>2</td>
<td>7</td>
<td>9 (8.9)</td>
</tr>
<tr>
<td>Total n (%)</td>
<td>56 (55.4)</td>
<td>35 (34.7)</td>
<td>10 (9.9)</td>
<td>101</td>
</tr>
</tbody>
</table>

UN: undernutrition.
Kappa index = 0.787 (IC: 0.670-0.897).
X² = 9.82, p = 0.001.
The usefulness of the analytical parameters for nutritional screening has been widely discussed. In the past, they were commonly used for this purpose, combined with other analytical information (IRN, IPN, etc.). In the last years they have been replace by nutritional screening tools based only on clinical information such as the SGA (recommended by the ASPEN), the NRS2002 (recommended by ESPEN) and the MUST (BAPEN). Nevertheless, all of these tools must be done through a direct interview and examination of the patient; therefore, they can hardly be applied to all inpatients and repeated during the hospital stay, so that this aspiration of the Council of Europe\(^3\) and the ESPEN\(^3\) considerably elevates staff numbers and time requirements.

The main reason for not using the analytical parameters in nutritional screening is that some authors made objections to these parameters as indicators of nutritional status when present in illness or aggressive treatment. For this reason, we wanted to study the behavior of the analytical parameters, specifically in these situations.

The three analytical parameters analyzed in this study have been selected among those more frequently used in clinical practice, to indicative the patient’s nutritional balance. The three of them show a good association with the nutritional status assessed by the SGA and FNA, so that as the levels of each one of the parameters get lower the patient’s undernutrition degree gets higher, as can be observed in tables IV and V.

The dynamics of the cut points adjust to what would be expected (table VII). The three parameters show a
considerably high sensitivity in the first cut point, and it is the albumin that, at this point, shows the maximum specificity (Alb $\geq 3.5$, sens = 0.89, spcf = 0.65). Total cholesterol and total lymphocyte count present, at that point, a much lower specificity value (0.46 in both cases). As it would be expected sensibility lowers for the three variables as the cut points go to lower values, and specificity increases to 1 in the case of albumin $\geq 2.5$ mg/dL. The choice of any of the cut points will depend upon how these parameters will be used.

As it can be observed in figure 2, the three parameters show a wide area under the curve (AUC), which indicates that their precision in detection of undernutrition is good.

Many authors reject albumin as an indicator of nutritional status, due to its long midlife (20 days). In clinical practice that midlife shortens immediately depending upon the seriousness of the clinical process. A hemorrhage or lymphorrhage can cause a dramatical decrease in minutes of the albumin level, as it falls in hours in a surgery or a chemotherapy or steroid treatment. Another reason to reject the use of albumin, is that serum albumin levels can be affected by many factors other than malnutrition such as inflammation, some drugs (corticosteroids, insulin, thyroid hormone, etc.) renal and liver disease, all of which result in a low sensitivity and specificity to changes on nutritional intake. Many studies have demonstrated the predictive value of hypoalbuminemia for morbidity, mortality, increase of LOS (length of stay) and costs. Therefore, hypoalbuminemia is often considered as an indicator of the illness severity rather than the nutritional status. However, there is an indirect relationship between inflammation (and the consequent hypoalbuminemia) with nutritional status. Inflammation contributes to an increase in net protein loss caused by catabolism, and also induces anorexia, reducing the probability that a patient will get an adequate intake to his requirements, thus accelerating the undernutrition process. In the present study, we have found a direct and significant relationship between serum albumin and nutritional status, which agrees with other literature reports. For this reason, even though serum albumin can be affected by many others non nutritional factors (illness, hospitalization or therapeutic treatments) it presents a strong relationship with nutritional status, and therefore it can not be ruled out for use in nutritional screening.

In this study, we suggest total cholesterol as an indicator of the patient’s energetic reserves, as the illness and therapeutical procedures frequently compromise the patient’s caloric balance. When the patient presents a caloric malnutrition, a weight loss and a drop in the BMI are observed. In our clinic experience we have observed
how serum cholesterol lowers at caloric depletion, even before a weight loss or other anthropometrical changes can be observed. We have found a relationship between total cholesterol and BMI and the percentage of weight loss (table VI), which would confirm its usefulness as an indicator of the patient’s caloric reserves.

Undernutrition induces immunological changes, such as a drop in total lymphocyte count, which increases frequency and severity of infection. This accounts for much of the morbidity and mortality associated with malnutrition. Total lymphocyte count has been suggested as a useful indicator of the nutritional status and outcomes, and it is quickly done and appropriate for all age groups.31-33

BMI is frequently used as an indicator of a patient’s nutritional status, considering lack of undernutrition if BMI > 20. We think that BMI itself is not a good indicator of nutritional status. When analyzing the results obtained in the present study, it can be observed that 80.2% of patients have a BMI > 20, and only 10.4% have a BMI < 18, while the prevalence of undernutrition found by SGA is 44%. Results concerning percentage of weight loss are closer to the prevalence of undernutrition in our study, since 46% of the patients referred lost weight. Therefore, SGA is more useful than BMI to detect undernutrition. These results are in agreement with other studies.34

Apart from their sensibility and specificity rates, a remarkable advantage of the analytical parameters for nutritional screening is that they are already available in every patient’s clinical file, this information is obtained at admission, during the hospital stay and during treatment. When planning the use of nutritional screening parameters, one must go to the clinical data bases to retrieve the information. Specific software could be utilized by clinicians to obtain nutritional risk measurements. The need for further nutritional assessment and/or needed intervention would be immediately determine. Depending on the result of the screening’s result, further nutritional assessment and early and adequate nutritional intervention can be done.

Conclusions

Analytical parameters analyzed in this study show a statistically significant relationship with the nutritional status evaluated by SGA and FNA. Total cholesterol correlates with BMI and percentage of weight loss, and therefore it can be consider as an indicator of caloric undernutrition. The results obtained in the present study support the use of the analytical parameters in computer screening tools for the early detection of undernutrition.

For these reasons, we propose bringing back the use of analytical parameters along with computer tools for automatic screening of patient undernutrition. With the computer tools it is possible to reach a larger number of patients during their entire clinical process. The tools permit quick and easy detection of variations during treatment as well as patient complications. What we propose would result in saving of money, personnel, and time for the hospital. In addition to its efficiency, this approach would be more patient friendly.

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