Can Nutritional Criteria Help Predict Outcome in Hospitalized Patients?

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The following nutritional criteria were evaluated for their usefulness in predicting outcome in a prospective study of 66 randomly selected hospitalized patients with a variety of diagnoses: total protein, albumin, and transferrin concentrations in serum, creatinine height index, weight height index, phenylalanine/tyrosine ratio (Phe/Tyr), concentration of branched-chain amino acids in serum, and ratio of essential to nonessential amino acids in serum. The cases were followed from admission to discharge, and were classified into the following three groups: 43 "well"; 14 with "complications" but recovered; and nine "dead." Statistical analysis (Scheffe's $s$-test) demonstrated the means of "well" and "dead" groups to be different for total protein, albumin, transferrin, and Phe/Tyr. In individual patients the nutritional criteria, even for those with fatal outcome, were poor indicators of outcome. These nutritional criteria are useful in identifying hospitalized groups that are at maximum risk (i.e., death), but are much less useful for individual patients.

Additional Keyphrases: total protein • albumin • transferrin • creatinine • weight height index • amino acids

Protein calorie malnutrition is common in hospitalized patients (1). Some studies indicate nutritional indices to be effective predictors of hospital morbidity and mortality that is secondary to protein calorie malnutrition (2, 3), but others find this not to be the case (4). Therefore, there is a need further to evaluate nutritional indices with respect to outcome in hospitalized patients with different disorders.

A wide array of indices is available for nutritional assessment. We chose to study those that had most or all of the following characteristics: not too narrowly available, economical to perform, and involving minimal trauma or discomfort to the patient. The nutritional criteria we studied include total protein, albumin, and transferrin in serum, creatinine height index (CHI), weight height index (WHI), and serum amino acids. The assay of serum amino acids is not inexpensive; it may also not be as easily or readily available as at our center.

Patients and Methods

Sixty-six hospitalized patients were included in the study: 31 women and 35 men, ages 16 to 84 years. Their diagnostic categories were as follows: major cardiac surgery, 17; major surgery, noncardiac, 19; trauma and orthopedics, 12; malignancies, 12; and others, six. The patients with malignancies were admitted for procedures such as radium implants. The patients were chosen without conscious bias from hospital admission records. The study protocol was permitted by The General Hospital Human Investigations Committee, and informed consent was obtained from each patient during the first 24 h after admission. None of these patients was receiving blood products, total parenteral nutrition, or therapy with amino acids.

Weight and height measurements, 24-h urine collections for creatinine assay, and serum sampling for albumin, transferrin, and amino acid analysis were completed by 48 h after admission. Albumin was assayed by the bromcresol green dye-binding method in a random-access analyzer (Hitachi 705). Transferrin was measured by radial immuno-diffusion with use of plates from Kallestad Canada Inc., Montreal, Quebec, Canada. Urinary creatinine was measured by a rate reaction Jaffe method in a random-access analyzer (Astra 8). Serum for amino acid assay was free of hemolysis and was stored at $-20^\circ$C until analysis; after deproteinization with sulfosalicylic acid, we assayed amino acids with a Beckman Model 121-MB amino acid analyzer.

From the serum amino acid profile we calculated the following indices: phenylalanine/tyrosine ratio (Phe/Tyr), total concentration of branched-chain amino acids (BCAA; includes isoleucine, leucine, and valine), and essential/nonessential amino acid ratio (E/NE; essential amino acids are threonine, valine, leucine, and lysine; nonessential amino acids are serine, glutamine, proline, and glycine). The cases were then followed to the time of discharge or death.

The same nutritional indices were also measured in 28 apparently healthy volunteers, all of them hospital employees, mostly laboratory technologists.

Results and Discussion

Table 1 lists the mean, 2 SD, and reference range for the nutritional criteria studied in the 28 healthy volunteers.

The mean stay for the hospitalized patients was 22 days (range, three to 117 days). Of the 66 patients, 43 had an uneventful stay and were discharged home ("well"), 14 developed complications but had overcome these at the time of discharge ("complications"), and nine patients died ("dead"). Among the nine patients who died there was a total of 18 complications: seven major septic, one minor septic, and 10 nonseptic. Among the 14 patients with complications who recovered there was a total of 21 compli-
cations: four major septic, nine minor septic, and eight nonseptic complications. Diagnostic group, age, sex, or length of stay did not influence inter-group differences with respect to morbidity and mortality, for the cohort of patients we studied (most of whom were older than 50 years).

The nutritional parameters were analyzed by one-way analysis of variance, and significant results were tested by Scheffe's s-test to compare the average for each group of patients. There were significant differences between the means for the "well" and "dead" patient groups for the following: total protein, albumin, transferrin, and Phe/Tyr (Table 2). However, for all the indices we tested, the wide scatter of individual data points about the mean resulted in poor sensitivity and specificity. Consequently, none of the indices was of much use in assessing an individual patient's nutritional status. These results accord with those of others (5, 6).

Albumin values for most of these patients were clustered around 32 (SD 4) g/L. Albumin is a negative acute-phase reactant: the albumin concentration in serum declines with onset of acute illness or trauma and remains low for a long time, owing to its long biological half-life of 20 days (7). Increase in vascular space and with extracellular volume further decrease serum albumin concentration (8). Transvascular or, more specifically, transcapillary escape rate is increased by 300% in septic shock and by up to 200% within the first 4 h after cardiac surgery (9). Therefore, albumin can be expected to be a poor indicator of protein calorie status in an individual patient, as indeed we found it was. Authors (e.g., 10) who used albumin cutoff values to ascertain protein calorie malnutrition may not have taken all of these factors into account.

Serum transferrin, with use of a cutoff point of 2.3 g/L, was reasonably sensitive and specific in distinguishing the "well" group from the other two groups, but again, values were widely scattered. This protein is affected by different physiological and pathological states, being low in anemia of malignancy, anemia of chronic disease, and cirrhosis of the liver, and high in iron-deficiency anemia, in pregnancy, and in women who are taking oral contraceptive pills. It has a relatively short half-life, eight to 10 days, and the extracellular pool is small, approximately 4 g. Serum transferrin concentrations decrease rapidly during the acute-phase response and remain low during chronic illness (11).

The data on CHI had a wide scatter, both in the healthy population and the hospitalized patients. We believe the 24-h urine collections to be accurate but we are unable to explain the unexpectedly wide scatter and the lack of efficiency of CHI in distinguishing the different groups.

WHI had a narrower range in the healthy population but was useless for differentiating the different groups of patients, most of the patients in the "complications" and "dead" groups having values within the normal reference interval.

Some investigators offer prognostic nutritional index (PNI) as a way of getting around the lack of efficiency of individual nutritional parameters (12, 13). PNI is a composite value derived from certain predetermined nutritional indices by complicated computer analyses. Many different PNIs have been recommended, attesting to their lack of general acceptance and difficulty of application in practice, unless persons or units with special interest in nutrition are available for consultation.

Means for Phe/Tyr in the "well" and "dead" groups differed significantly, but the values for the "well" and "complications" groups overlapped a little. However, most patients in the "dead" group had a high Phe/Tyr ratio.

Increased Phe/Tyr could be due to (a) increased release of phenylalanine from muscle breakdown, (b) decreased conversion of phenylalanine to tyrosine in the liver, (c) increased rate of phenylalanine absorption by the kidneys, (d) decreased utilization of phenylalanine for protein synthesis (14), or some combination of these.

We were unable to demonstrate differences in the means for BCAA and ENE in the three groups, although BCAA was high in a large majority of the patients in the "well" group. Very low BCAA concentrations indicate a poor prognosis, which forms the basis of BCAA infusions in various traumatic and septic states to improve prognosis by satisfying muscle-energy requirements (15).

In conclusion: we find transferrin, albumin, total protein and Phe/Tyr to be useful in identifying the hospitalized group at risk of death, but there is a significant overlap of values, particularly between the "well" and "complications" group. Thus, individual data on individual patients lack efficiency. Derivation and use of PNI may be useful in centers with units or persons offering consultative service in nutrition. Clinical evaluation is a very valuable tool, always to be used in nutritional assessment. However, the search for specific nutritional markers continues—especially retinol-binding protein, transthyretin (prealbumin), and fibrinectin. These assays are currently not available at our center and therefore could not be evaluated in this study.

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References
Two-Site Enzyme Immunoassay for Alpha-Fetoprotein in Dried-Blood Samples Collected on Filter Paper

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This is a method for measuring alpha-fetoprotein (AFP) in eluates of dried-blood samples on filter paper by use of a simple, sensitive two-site enzyme immunoassay. The spot, 6 mm in diameter (equivalent to about 12 μl of whole blood), is incubated overnight with alkaline phosphatase conjugated to rabbit anti-AFP antibody in a tube containing a polystyrene bead coated with mouse monoclonal antibody to AFP. After the beads are washed the enzyme activities associated with them are determined colorimetrically, with p-nitrophenyl phosphate as substrate. The measurable range of AFP is from 9 to 900 μg per liter of plasma. AFP in the dried-blood spot as determined by this method correlated well with the AFP value for serum from the same blood sample as determined by radioimmunoassay (r = 0.957, p < 0.001). Preliminary studies in which we used this method with 242 healthy blood donors and 60 patients with hepatocellular carcinoma indicate that it may be suitable for use in mass screening for hepatocellular carcinoma in high-risk populations.

Additional Keyphrases: screening · liver disease · cancer · radioimmunoassay of serum compared · cutoff value

Abelev et al. (1), in 1963, first reported the observation of increased alpha-fetoprotein (AFP) in the serum of mice bearing transplanted hepatocellular carcinoma. In the following year, Tatarinov (2) discovered increased values for AFP in patients with hepatocellular carcinoma. Since then, AFP has become one of the best-studied oncofetal proteins.

Materials and Methods

Reagents. Alpha-fetoprotein was purified from pooled human cord blood as described by Wu et al. (8). A human AFP standard (72/225) was kindly supplied from the International Laboratory for Biological Standards, World Health Organization, Copenhagen, Denmark, and additional AFP standards were purchased from Dako Corp., Santa Barbara, CA 93103. Alkaline phosphatase was obtained from Behringer Mannheim GmbH, Mannheim, F.R.G. Bovine serum albumin, p-nitrophenyl phosphate, and diethylaminoethyl-(DEAE)-cellulose were from Sigma Chemical Co., St. Louis, MO 63178. Special filter paper for use in neonatal screening was from Toyo Kagaku Sangyo Co., Tokyo, Japan. Polystyrene beads (6 mm) were from Precision Plastic Co., Chicago, IL 60641. Sepharose 6B, CNBr-activated Sepharose 4B, and Sephadex G-200 were from Pharmacia Fine Chemicals, Uppala, Sweden. All other chemicals were of the highest quality obtainable.