Specificity of indexes of malnutrition when applied to apparently healthy people: the effect of age[1–3]

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ABSTRACT Protein-energy malnutrition is thought to be widespread in hospitalized patients. However, the specificity of indexes used to assess malnutrition is uncertain. We therefore assessed the rate of false-positive diagnoses of malnutrition when biochemical-anthropometric indexes were applied to healthy subjects. Nutritional status was assessed in 175 healthy blood donors (aged 44.2 ± 13.4 y) and in 34 highly fit elderly volunteers (aged 74.7 ± 3.6 y) participating in the Nijmegen Four Days Walking March. We investigated both the Nutritional Risk Index [(1.489 × albumin) + (41.7 × present/usual weight)] and the Maastricht Index [20.68 − (0.24 × albumin, g/L) − (19.21 × serum transthyretin, g/L) − (1.86 × lymphocytes, 10^6/L) − (0.04 × ideal weight)]. We found previously that 52–64% of nonsurgical hospitalized patients were malnourished according to these indexes. In the present study, 1.9% of the 209 volunteers had apparent malnutrition according to the Nutritional Risk Index and 3.8% according to the Maastricht Index. The prevalence of apparent malnutrition in the elderly volunteers was 5.9% and 20.6%, respectively. The rate of false-positive diagnoses was acceptably low in those aged < 70 y with both the Nutritional Risk Index and the Maastricht Index; therefore, the use of these indexes will not cause a clinically significant increase in the prevalence of malnutrition because patients who are not malnourished are included. The high percentage of spurious malnutrition in the elderly limits the use of the Maastricht Index to subjects aged < 70 y. *Am J Clin Nutr* 1997;65:1721–5.

KEY WORDS Nutritional status, validation, biochemistry, anthropometry, nutritional indexes, Nutritional Risk Index, Nutrition Index, elderly, Maastricht Index, protein-energy malnutrition, transthyretin, prealbumin, humans

INTRODUCTION

Various methods have been developed to assess protein-energy malnutrition in hospitalized patients. In 20 published studies the observed frequency of malnutrition varied from 23% to 62%, with an overall mean of 38% (**Table 1**). In a previous study in nonsurgical hospitalized patients we found a prevalence of malnutrition of 52% using the Nutritional Risk Index and 64% using the Nutrition Index, otherwise known as the Maastricht Index (19). The Nutrition Index was developed by workers in Maastricht, Netherlands; to avoid confusion with similarly named indexes we will call it the Maastricht Index in this paper. In malnourished surgical patients assessed with these indexes, nutritional intervention has proven to reduce the number of postoperative complications (20–22). If the prevalence of malnutrition is truly high in nonsurgical patients, a considerable percentage of these patients might also benefit from nutritional support. However, the specificity of current instruments for assessing malnutrition has not been assessed properly. The Nutritional Risk Index was developed by calculating the association of various nutritional indexes with postoperative complications (23, 24). The Maastricht Index was developed by comparing objective nutritional indexes in 50 patients selected for parenteral nutrition with the same indexes in 38 patients selected for elective minor surgical procedures (25). Neither of these indexes have been validated in healthy subjects. We were concerned about whether the high prevalence of protein-energy malnutrition that we observed in nonsurgical hospitalized patients could originate from false-positive misclassification. We therefore investigated the prevalence of apparent malnutrition in a healthy population, in whom the prevalence of true malnutrition should have been low.

SUBJECTS AND METHODS

Subjects

The study was performed after permission had been obtained from the Committee for Ethics and Research in Humans. We selected 175 blood donors and 34 healthy elderly people. In the Netherlands blood donors give blood at least once or twice a year as an act of charity without financial compensation. All donors are registered and receive medical and laboratory checkups at regular intervals. Only volunteers who were completely healthy, according to their most recent medical and laboratory checkup, and free of active or chronic diseases were

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TABLE 1
Published figures for the prevalence of malnutrition in random samples of hospitalized patients

Patients and reference	Prevalence[1]
	%
Surgical	
Postma and Wesdorp (1)	23 [422]
Hall (2)	29 [367]
Pettigrew et al (3)	32 [198]
McWhirter and Pennington (4)	33 [200]
Bistrian et al (5)	40 [131]
Detsky et al (6)	44 [202]
Reilly et al (7)	48 [406]
Buzby et al (8)	62 [100]
Mean	41
Geriatric	
Larsson et al (9)	29 [500]
Füllöp et al (10)	34 [552]
Constans et al (11)	37 [324]
Sullivan and Carter (12)	38 [110]
Mean	33
General medicine	
Larsson et al (13)[2]	29 [382]
Willard et al (14)[2]	32 [200]
Coats et al (15)	38 [228]
McWhirter and Pennington (4)	45 [300]
Weinsier et al (16)	48 [134]
Robinson et al (17)	56 [100]
Reilly et al (7)	59 [365]
Bistrian et al (18)	44 [251]
Mean	44

[1] n in brackets.
[2] Part of the sample were also surgical patients.

selected for this study. Their mean (± SD) age was 44.2 ± 13.4 y and their body mass index (BMI: in kg/m^2) was 25.6 ± 4.1.

In the Netherlands persons aged ≥ 70 y are excluded from blood donorship. We therefore approached elderly people who had completed the 1993 Nijmegen Four Days Walking March, a sports event in which volunteers walk 30 km (≈19 miles) each day for 4 d (**Table 2**). We excluded elderly persons suffering from a chronic disease, thereby reducing the risk of including malnourished persons. The remaining 34 elderly subjects had a mean (± SD) age of 74.7 ± 3.6 y and a BMI of 24.1 ± 2.3. The age distribution of subjects was similar to that of the hospitalized patients whom we studied previously (19) (Table 2).

TABLE 2
Characteristics of 209 healthy Dutch volunteers investigated for the prevalence of apparent malnutrition

Age range (y)	Number of women	Number of men	Height	Weight
			cm	*kg*
21–29	18	17	176 ± 8.5[1]	74.7 ± 12.2
30–39	17	18	173 ± 9.6	73.1 ± 12.3
40–49	17	18	172 ± 8.4	77.0 ± 15
50–59	19	16	169 ± 8.1	79.2 ± 11.8
60–69	16	21	169 ± 9.3	74.3 ± 11.4
> 69	11	21	168 ± 8.2	69.1 ± 10.4
Total	98	111	171.2 ± 8.7	74.6 ± 12.2

[1] $\bar{x}$ ± SD.

TABLE 3
Indexes used to determine the nutritional status of 209 healthy volunteers

Nutritional Risk Index (23, 24) = (1.489 × serum albumin, g/L) + 41.7 × present weight/usual weight)

> 100: not malnourished
97.5–100: mild malnourishment
83.5 to < 97.5: moderate malnourishment
< 83.5: severe malnourishment

Maastricht Index (25) = 20.68 − (0.24 × serum albumin, g/L) − (19.21 × serum transthyretin, g/L) − (1.86 × lymphocytes, 10^6/L) − (0.04 × ideal weight)[1]

≤ 0: not malnourished
> 0: malnourished

[1] Ideal weight was determined by using Metropolitan Life Insurance Company tables (26).

Assessment of nutritional status

We used two methods to determine nutritional status: the Nutritional Risk Index (23, 24) and the Maastricht Index (25) (**Table 3**). The Nutritional Risk Index is based on serum albumin concentrations and present compared with usual weight; a value ≤ 100 indicates malnutrition. The Maastricht Index uses serum albumin, serum transthyretin (prealbumin), blood lymphocyte count, and percentage of ideal weight; a positive value indicates malnutrition. Metropolitan Life Insurance Company tables were used to determine ideal weight (26).

Current weight was determined with a Krupps (Solingen, Germany) or a Seca (Hamburg, Germany) balance, and height with a Seca or Stanley 04–116 microtoise (Stanley Tools, New Britain, CT). The usual weight for blood donors was the weight registered by the blood bank 6 mo before the assessment of nutritional status; the usual weight was also ascertained in all subjects with a questionnaire. The weight reported by the blood donors and the weight recorded by the blood bank 6 mo before the assessment were similar (75.0 ± 12.2 and 75.4 ± 12.8 kg, respectively).

Laboratory methods

Blood albumin concentrations and other analyses are influenced by body posture (27). Therefore, blood sampling was performed with subjects in a semirecumbent position identical to that used in patients in our clinical study and in most hospitals (22). In the elderly people blood was drawn before or ≥ 2 wk after the Nijmegen Four Days Walking March. Training was performed ≈5 h/wk. To exclude influences of training on blood albumin concentrations and other analyses, the elderly volunteers were asked not to train for ≥ 2 d before blood sampling.

Serum albumin concentrations were determined by spectrophotometry with bromcresol green on a BM/Hitachi 747 analyzer (Hitachi, Tokyo), transthyretin by immunonephelometry on a Cobas Fara II analyzer (Hoffmann-La Roche, Basel, Switzerland) using a rabbit antihuman transthyretin antiserum (DAKO, Copenhagen). Transthyretin was calibrated against

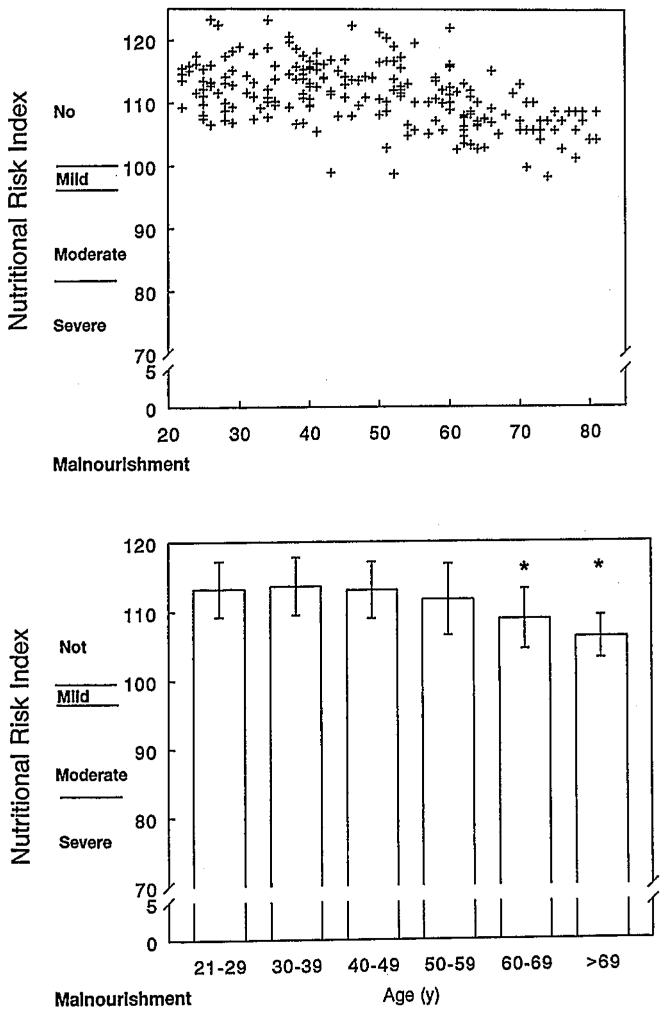

FIGURE 1. Individual Nutritional Risk Index values by age (top) in 209 apparently healthy subjects and mean (± SD) Nutritional Risk Index values by age category (bottom) in 209 apparently healthy subjects. *Significantly different from the age category 21–29 y, $P < 0.05$.

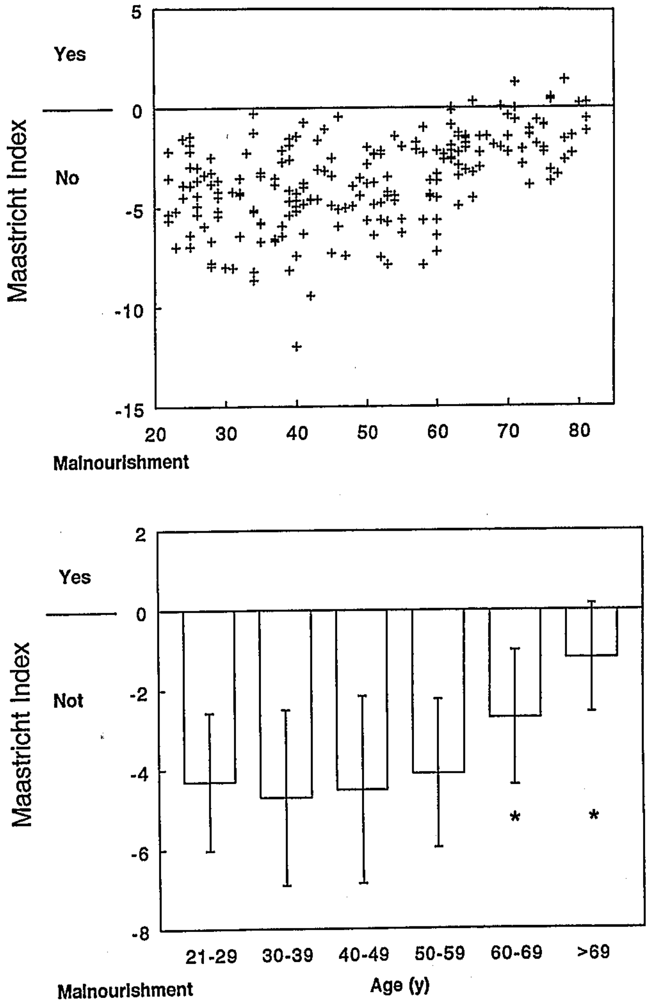

FIGURE 2. Individual Maastricht Index values by age (top) in 209 apparently healthy subjects and mean (± SD) Maastricht Index values by age category (bottom) in 209 apparently healthy subjects. *Significantly different from the age category 21–29 y, $P < 0.05$.

CRM (Certified Reference Material)-470 international reference serum of the International Federation of Clinical Chemistry. The total number of blood lymphocytes was determined with an automatic cell counter (Sysmex NE 8000; TOA Medical Electronics, Kobe, Japan).

Statistics

We made the assumption that in a healthy population the true prevalence of malnutrition is 0%. The observed percentage of malnourished persons in our sample therefore equaled the percentage that was misclassified. The upper limit of the 95% CI for the proportion malnourished was calculated as follows:

$$p + Z_\alpha \times SD(p), \text{ where } SD(p) = \sqrt{[p(1-p)/n]} \qquad (1)$$

where p is the observed proportion malnourished, n is the sample size, and Z_α is 1.96. For the subgroup of elderly subjects, 95% CIs were calculated by using tables for small samples (28). All calculations were made with the statistical program SAS (29).

RESULTS

The mean (± SD) Nutritional Risk Index value for the total sample was 111.1 ± 4.9. Four of the 209 volunteers were classified as mildly malnourished (97.5–100) according to the Nutritional Risk Index: two were men and two women, and three of the four were aged > 50 y. The apparent percentage of malnutrition was thus 1.9% (upper limit of the 95% CI: 3.8%). Mean (± SD) Nutritional Risk Index values by age are shown in **Figure 1**. Three of the subjects were classified as malnourished because of a minor decrease in serum albumin. However, the weight of these three persons was > 100% of their usual weight. Their present weight was 171.2 ± 8.7 kg (Table 2); in 52% of the subjects it was lower and in 48% it was higher than their usual weight. One male weighed 87% of his usual weight and was classified as malnourished according to the Nutritional Risk Index; nevertheless, his actual weight was higher than his ideal weight according to Metropolitan Life Insurance Company tables (26). This person was the fourth one categorized as malnourished according to the Nutritional Risk Index. The outcome for the age categories of 60–69 y and > 69 y was significantly lower than that for ages 21–29 y, indicating an increased apparent risk at a higher age. The mean prevalence of apparent malnutrition in the blood donors aged 21–69 y was 1.1% (upper limit of the 95% CI: 2.7%), as opposed to 6% (upper limit of the 95% CI: 20%) in the elderly hikers who were aged > 69 y. No significant differences were observed between sexes.

The mean Maastricht Index value for the total sample was −3.63 ± 2.25 (**Figure 2**). Nine subjects, or 4.3% (upper limit of the 95% CI: 7.0%), were classified as malnourished according to the Maastricht Index; seven were males and all nine were aged > 60 y (Figure 2). The reasons for apparent malnutrition according to the Maastricht Index were a combination of factors in all cases. A significantly higher (ie, poorer) score for this index was seen in the age categories 60–69 y and > 69 y compared with the reference age category of 21–29 y, again indicating a higher probability of spurious malnutrition at a higher age. The mean prevalence in the blood donors was 1.1% (upper limit of the 95% CI: 1.2%) and in the elderly walking competitors it was 20.6% (upper limit of the 95% CI: 38%). No significant differences were seen between sexes.

DISCUSSION

We applied two biochemical-anthropometric indexes to assess clinical malnutrition in two groups of healthy subjects and found that the rate of apparent malnutrition was low and of no clinical significance in the group of subjects aged < 70 y; however, 6–21% of our group of highly fit, active elderly subjects were classified as malnourished.

We assumed that the volunteers were not malnourished. This was plausible because of the process by which the volunteers were selected: a medical and laboratory examination showed no abnormalities, and volunteers with chronic diseases were excluded. In the Netherlands blood donors are unpaid, and donorship is seen as an act of charity. The volunteers were socially well adjusted, had a regular income, and were of normal body weight on the basis of their BMI. In our group of elderly volunteers, BMI was not significantly different from that in younger volunteers. It is well known that elderly subjects not selected on the basis of health status, nutritional habits, or lifestyle factors can be malnourished with regard to protein (30) and micronutrients. In most previous studies concerning malnutrition in elderly persons, subjects with chronic diseases were not excluded. If they were excluded the proportion of malnourished elderly persons was < 10% (31). The group of elderly volunteers included in our study was physically active and their average nutrient intake was close to Dutch recommendations (32). However, although we tried to select only persons who were not malnourished for this study, we could not guarantee that none were malnourished because the selection process is fallible.

One could argue that some of the variables used in these indexes are derived from laboratory methods that have been calibrated to yield normal values in a normal healthy population, so that the outcome is biased to normal values. However, the coefficients and constants that are used to calculate the value of each index are fixed and not calibrated per laboratory. The published reference ranges could be inapplicable, and the outcome of the index could be erroneous if the coefficients and constants used are inappropriate for the population studied. Therefore, apparent prevalence of malnutrition in healthy volunteers could be considerable. This is illustrated by the discrepancy in frequency between the two indexes. The less favorable values seen in our otherwise highly fit elderly subjects might suggest that some of them were malnourished despite our various precautions to avoid the selection of malnourished individuals. It could also suggest that the risk of a misdiagnosis of malnutrition is appreciable in elderly patients. On the basis of the Nutritional Risk Index, the percentage of apparent malnutrition in our highly fit elderly subjects aged ≥ 70 y was 6% with an upper limit of the 95% CI of 20%; using the Maastricht Index it was 21% with an upper limit of the 95% CI of 38%. These figures raise questions about the clinical significance of nutritional indexes when applied to elderly subjects. A false diagnosis of malnutrition could cause a patient to receive unnecessary enteral or parenteral nutrition, which is expensive and could induce complications.

The two elderly volunteers categorized as malnourished on the basis of the Nutritional Risk Index were both classified as mildly malnourished. Obviously, the risk of a false-positive diagnosis is highest in subjects classified as mildly malnourished. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group showed that perioperative parenteral nutrition was ineffective in such mildly malnourished patients, and was effective only in more severely malnourished patients (21). Therefore, the consequence of misclassification of elderly patients with this index is limited. The Maastricht Index does not include grades of malnutrition and use of this index in elderly patients resulted in ≥ 21% of the elderly patients being treated mistakenly for malnutrition. However, the number of elderly subjects in our study precludes definitive conclusions.

Our results indicate that the high proportion of hospitalized patients diagnosed as malnourished is not due to positive misclassification, except possibly when elderly patients are involved.

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