Are Elderly Hospitalized Patients Getting Enough Protein?

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OBJECTIVES: To determine the protein requirements of elderly hospitalized patients.

DESIGN: Cross-sectional evaluation of nitrogen balance.

SETTING: Short-stay geriatric ward or rehabilitation care unit.

PARTICIPANTS: Thirty-six elderly hospitalized patients (aged 65–99) admitted to short-stay and rehabilitation care units.

MEASUREMENTS: Resting energy expenditure and nitrogen balance were determined under usual and spontaneous energy and protein intake after subjects were clinically stable (3–5 days after admission). All items consumed over a 3-day period were weighed to determine energy and protein intake.

RESULTS: Energy (23.5 ± 6.3 kcal/kg per day) and protein (0.99 ± 0.24 g/kg per day) intake were similar in men and women, and nitrogen balance was neutral (0.37 ± 2.6 g/day; $P = .41$ vs a neutral nitrogen balance, i.e., 0 g/d). Half of the patients had a positive nitrogen balance. Plasma C-reactive protein, renal function, nutritional status, and initial diagnosis had no influence on nitrogen balance. In contrast, energy and protein intakes correlated positively with nitrogen balance. Linear regression analysis suggested that an elderly hospitalized patient with an energy intake of 1.31 times resting energy expenditure or greater appears to require a minimum protein intake of 1.06 ± 0.28 g/kg per day.

CONCLUSION: Mean protein intake to reach a neutral nitrogen balance in elderly hospitalized patients is 1.06 ± 0.28 g/kg per day, which is higher than current recommendations for healthy elderly people. Safe protein intake (that would be adequate to ensure that 95% of patients remain in positive nitrogen balance) is difficult to establish. **J Am Geriatr Soc 56:1045–1049, 2008.**

Key words: aging; protein requirements; nitrogen balance; resting energy expenditure; disease

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Proteins, key constituents of the body, play an essential role in tissue organization, muscle contraction, hormone synthesis, receptor development, immune defense, transport mechanisms, enzymatic activity, and metabolic regulation. Protein loss may therefore lead to major structural and functional changes in tissues, with immediate consequences for the health of the individual. Body protein mass is the result of a balance between protein intake and protein oxidation into urea and carbon dioxide. Inadequate protein intake will compromise functional status, muscle mass, and the body's capacity to recover from stress. This is why protein deficiency is an important determinant of morbidity and frailty, particularly in elderly hospitalized patients.

The dietary protein allowance recommended for elderly people by the 1985 joint Food and Agricultural Organization/World Health Organization/United Nations University (FAO/WHO/UNU) report[1] corresponds to a protein intake of 0.80 g/kg per day, although this figure is based on extrapolation of observations of healthy people of various ages, young and old. Some studies that have measured protein requirements in healthy elderly people[2–8] indicate values ranging from 0.80 to 1.25 g/kg per day. The large variation may be due to methodological differences in the studies and the small number of subjects.[9] One study[3] that reassessed these results concluded that healthy elderly people would require a minimum protein intake of 1.00 to 1.25 g/kg per day for nitrogen equilibrium.

As for elderly hospitalized patients, their protein requirements are not really known at all. There are many reasons why such patients should have a significantly greater protein intake than healthy elderly people. For instance, inflammation or infection can rapidly deplete body nitrogen stores. Thus, critically ill young people were found to require a protein intake of 2.50 g/kg per day before a positive nitrogen balance was restored.[10] A protein intake of 1.25 to 2.20 g/kg per day has been recommended for patients in intensive care units, regardless of age;[11] and for patients with pressure ulcers, a minimum protein intake of 1.75 g/kg per day has been recommended to improve healing.[12] Infectious conditions increase protein catabolism and divert amino acids toward the synthesis of acute-phase proteins in the liver and the immune system.[13] During inflammation and healing, the breakdown of muscle protein supplies amino acids to injured tissues and immune cells. This degradation leads to a negative nitrogen balance when protein

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intake is inadequate. Furthermore, one study has shown that up to 60% of patients admitted to the hospital may be malnourished,[14] whereas another has suggested that malnourished elderly people require a 30% higher protein intake than healthy elderly people.[15] For all these reasons, it would appear important to further investigate the protein requirements of elderly hospitalized patients.

The aim of this study was to estimate protein requirements for a group of elderly patients hospitalized in short-stay geriatric wards and rehabilitation care units. For ethical reasons, the classical method of measuring nitrogen balance by means of graded intake of nitrogen was inadvisable with frail, hospitalized patients. Therefore, a direct assessment of nitrogen balance under conditions of usual and spontaneous protein intake was used. Protein requirements were estimated for the whole group of frail, elderly, ill patients by interpolating the level of protein intake required to maintain nitrogen equilibrium.

PATIENTS AND METHODS

Protocol

Three-day nitrogen balance was measured in a subgroup of patients in whom energy metabolism was being investigated.[16] The ethics committee of the University Hospital of Angers approved the protocol of the study; all the patients gave informed written consent.

Patients

Men and women aged 65 and older and consecutively admitted to short-stay or rehabilitation care units were eligible for the study. Measurements were begun 4 days after admission to the hospital to ensure that the patients were in a clinically stable condition with a standardized food intake. Only patients free from incontinence and possessing sufficient cognitive capability (a Mini-Mental State Examination (MMSE) score >18) were invited to participate in the study. Medical history and disease status on admission were recorded for each patient, and a physical examination was performed the day before starting measurements.

Of the initial 110 patients recruited, 36 were retained for the study. The main reason for excluding the other patients was urinary incontinence, which was likely to compromise the full, 3-day urinary collection necessary for interpretation of nitrogen balance. A 1-day urinary collection was obtained from the 74 patients excluded from the study, and these patients did not differ from the 36 patients included in the study with respect to body mass index (BMI; 26.3 ± 5.9 vs 27.8 ± 5.8 kg/m^2, $P = .23$), protein intake per kilogram of body weight (0.98 ± 0.27 vs 0.99 ± 0.24 g/kg per day, $P = .85$), energy intake per kilogram of body weight (24.7 ± 7.1 vs 23.7 ± 6.4 kcal/kg per day, $P = .51$), and resting energy expenditure (REE) per kilogram of body weight (18.7 ± 3.0 vs 19.1 ± 2.3 kcal/kg per day, $P = .45$), although as a group, they were slightly older (81.0 ± 7.0 vs 77.4 ± 8.0, $P = .02$), and weighed less (71.3 ± 17.7 vs 64.3 ± 15.4 kg $P = .04$) than the patients who were included. Other factors, such as activities of daily living, central temperature, plasma electrolytes, kidney function, blood cell counts, albumin, and C-reactive protein (CRP) were similar in both groups of patient.

Anthropometry

On the first morning of the study, patients were weighed on a calibrated scale, and height was evaluated from the knee-to-heel length, as described previously.[17]

Nitrogen Intake

Nitrogen intake was assessed from a 3-day food weighing record while the patients were on ad libitum oral food intake with a standardized diet for at least 4 days. All food items, including snacks and drinks, were weighed before and after meals for 3 days. The same dietitian calculated the total daily protein intake (protein intake from all meals and snacks) of each of the patients using the French food composition tables (BILNUT 4.0. S.C.D.A., 1995, Nutrisoft, Cerelles, France). Energy intake was calculated in a similar way. Daily protein intake was then converted to nitrogen intake, assuming that 1 g of nitrogen corresponds to 6.25 g of protein.

Nitrogen Losses

Proteins are metabolized as urea, creatinine, uric acid, and other nitrogenous products that are excreted in the urine. Urinary urea represents 80% of the nitrogen excreted in the urine. Simultaneously with the 3-day weighing of food, a complete 72-hour urinary collection was made. The collection began on the first morning at 8:00 a.m., after voiding, and finished on the fourth morning at 8:00 a.m. Every 12 hours, a sample of urine was collected and frozen for later analysis of urinary urea. Urinary urea was quantified using a Hitachi 911 automat (Roche Diagnostics, Mannheim, Germany). Only complete 72-hour urine collections were used for data analysis. In addition to urinary nitrogen excretion, nitrogen is also lost in feces, reportedly at the rate of 18 mg/kg per day in elderly people.[2–8] Miscellaneous losses of nitrogen in sweat, sloughed skin, nails, hair, and various body secretions and excretions were assumed to occur at 8 mg/kg of body weight per day, as indicated by the 1985 joint FAO/WHO/UNU report.[1]

Nitrogen Balance

Nitrogen balance was calculated from the difference between daily nitrogen intake and total nitrogen losses. The protein requirement for hospitalized elderly people was obtained from the linear regression of nitrogen balance as a function of protein intake per kg of body weight. The level of protein per kilogram of body weight required to sustain a neutral nitrogen balance was taken to indicate the protein requirement.

Energy Expenditure

REE was measured in the fasting state using indirect calorimetry[18] on one of the 3-day periods during which intake was recorded. A ventilated hood system (Vmax Spectra, SensorMedics, Yorba Linda, CA) was wheeled to the patient's room. The system was calibrated before measurement in accordance with the manufacturer's instructions. With the patient in the supine position, a 40-L transparent Perspex hood was placed over the head and neck, with a thin plastic apron providing a rough seal around the chest. On the eve of the measurement, patients were asked to wear the hood above their head for 15 minutes so as to reduce any apprehension arising on the day of the measurement. To avoid acute stress that could invalidate the results, these measurements were begun a few days after hospitalization.[18] Recordings were made every 30 seconds for at least 30 minutes or until such time as a 15-minute steady-state period was observed; the data were then averaged to represent REE.

Blood Analyses

Blood was drawn from fasting patients before any other measurement was made on one of the 3 days during which food intake was recorded. The blood samples were centrifuged at 4°C and a 1-mL aliquot of plasma was rapidly frozen (−20°C) for subsequent analysis. CRP, plasma sodium, potassium, and creatinine concentrations were measured using a Hitachi 911 automat. Albumin was measured using turbidimetry. An inflammatory state was considered to exist when CRP level was greater than 9 mg/L.

Statistical Analysis

Results are expressed as means ± standard deviations (SDs). A one-way analysis of variance was used to assess the influence on the nitrogen balance of covariates (BMI (≤21 kg/m^2), inflammation (CRP ≥9 mg/L), renal function (normal renal function (creatinine clearance (CrCl) > 60 mL/min, mild renal insufficiency with a CrCl 30–60 mL/min, and severe renal insufficiency CrCl < 30 mL/min), and dementia (MMSE score 19–24)). Linear regression was used to interpolate for protein requirements. A univariate *t*-test was used to assess the statistical difference between mean and neutral nitrogen balances. The Kruskal-Wallis test was used to determine the influence of the initial diagnosis. In addition, univariate and multiple backward regression analysis was performed between nitrogen balance and the covariates listed above. The threshold of statistical significance was set at $P < .05$. Statistical computations were performed with the SPSS statistical package (SPSS Inc., Chicago, IL).

RESULTS

Patient Characteristics

Table 1 shows the characteristics of the 17 men and 19 women who participated in the study. BMI ranged from 15.5 to 40.0 kg/m^2. The weight of the patients was stable over the 5 days of the study (+0.04 ± 0.77 kg, $P = .74$). One patient had cardiac failure, two patients had moderate dementia, and the others had at least two of the following disorders: inflammation, infection, dementia, pressure ulcers, and respiratory and cardiac failure.

Nitrogen Balance

Table 2 shows intake of energy and macronutrients and nitrogen balance. Protein intake was higher in men than in women. Mean REE and energy intake were similar in men and women. Although energy intake was low, it was greater than REE by a factor of 1.24 ± 0.31 ($P = .001$).

Total daily nitrogen excretion was apparently higher in men than in women but was similar once adjusted for body weight (0.162 ± 0.038 g/kg per day, $P = .16$). Mean nitrogen balance (−0.37 ± 2.60 g of nitrogen per day, equivalent to −3.99 ± 36.07 mg/kg per day) was neutral ($P = .40$) and was similar in men and women ($P = .41$). Half of the patients had a positive nitrogen balance. Six men and seven women had a nitrogen balance less than −1 g/day, and five men and five women had a nitrogen balance greater than +1 g/day. Six men and seven women had a nitrogen balance between −1 and +1 g/d.

Figure 1 shows the positive relationship between individual nitrogen balance and nitrogen intake. Nitrogen

Table 1. Characteristics of the 36 Patients Studied

Characteristic	All Subjects	Men (n = 17)	Women (n = 19)
	Mean ± Standard Deviation		
Age	77.4 ± 8.0	75.2 ± 6.9	79.5 ± 8.5
Weight on the day before the beginning of the measurements of nitrogen balance, kg	71.3 ± 17.7	76.7 ± 19.0	66.5 ± 5.3
Height, m	1.60 ± 0.09*	1.65 ± 0.10	1.55 ± 0.05
Body mass index, kg/m^2	27.8 ± 5.8	27.8 ± 5.4	27.7 ± 6.3
Resting energy expenditure/kg of body weight, kcal/kg per day	19.1 ± 2.3	18.9 ± 2.1	19.3 ± 2.5

* $P < .001$ between men and women.

Table 2. Energy, Nitrogen Balance, and Macronutrient Intakes

Energy, Nitrogen Balance, and Macronutrient Intake	All Subjects	Men (n = 17)	Women (n = 19)	Sex Effect (*P*-Value)
	Mean ± Standard Deviation			
Energy intake, kcal/kg per day	23.5 ± 5.4	23.7 ± 6.6	23.4 ± 6.3	.09
Carbohydrate intake, %	46.7 ± 7.0	45.3 ± 5.7	47.9 ± 7.8	.03
Lipid intake, %	36.0 ± 5.8	35.9 ± 5.1	36.0 ± 6.5	.10
Protein intake, %	17.3 ± 3.1	18.8 ± 2.7	16.0 ± 2.9	< .001
Protein intake, g/kg	0.99 ± 0.24	1.07 ± 0.24	0.91 ± 0.23	.005
Nitrogen intake, g/d	11.0 ± 3.2	12.8 ± 3.1	9.5 ± 2.4	.005
Nitrogen output, g/d	11.4 ± 3.2	12.8 ± 2.4	10.2 ± 3.4	.001
Urinary nitrogen loss, g/day	9.6 ± 2.9	10.8 ± 2.1	8.5 ± 3.2	.001
Estimated fecal nitrogen loss, g/day	1.28 ± 0.32	1.38 ± 0.34	1.20 ± 0.27	.008
Estimated miscellaneous nitrogen loss, g/day	0.57 ± 0.14	0.61 ± 0.15	0.53 ± 0.12	.008
Nitrogen balance, g/day	−0.37 ± 2.60	0.02 ± 2.74	−0.72 ± 2.50	.04

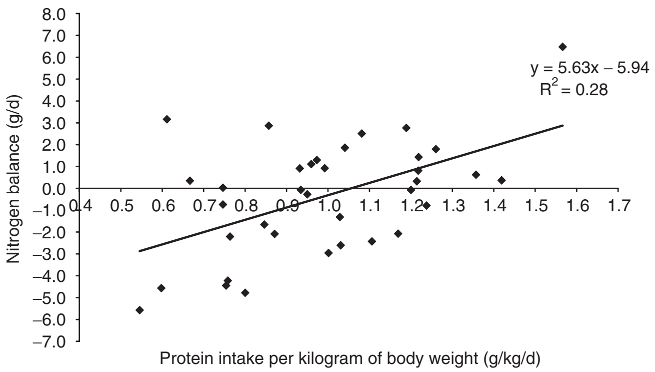

Figure 1. Relationship between individual nitrogen balance and nitrogen intake.

balance was positively correlated with protein intake (expressed per kg of body weight; $P = .001$, correlation coefficient (r) = 0.52). The relationship nitrogen balance (g/d) = $5.63 \times$ protein intake (g/kg body weight/day) − 5.95 was used to determine that the minimum protein intake for nitrogen equilibrium in the group of elderly hospitalized people would be 1.06 ± 0.28 g/kg.

The ratio of energy intake to REE correlated positively with nitrogen balance ($P = .009$, $r = 0.447$). The coefficient of linear regression suggested that a minimal ratio of 1.31 would be required for a neutral nitrogen balance in patients consuming 0.99 g/kg per day of protein. Because of the covariance between protein and energy intake, this intake did not determine nitrogen balance after protein intake was included in the model.

Nitrogen balance did not differ with nutritional status (BMI $\geq$ or <21 kg/m^2; $P = .83$). Mean plasma CRP of 18.5 ± 27.8 mg/L was uncorrelated with nitrogen balance ($P = .08$). The difference in nitrogen balance between subjects with inflammatory conditions (CRP > 9 mg/L) and those without did not reach statistical significance (0.39 ± 2.73 vs -1.05 ± 2.35 g/day; $P = .10$). In addition, initial diagnosis ($P = .26$), renal function ($P = .30$), REE level ($P = .36$), and presence of dementia (MMSE score 19–24) ($P = .53$) did not influence nitrogen balance.

DISCUSSION

To the best of the authors' knowledge, no data have been published on the protein and energy requirements of elderly hospitalized patients. Observations of a group of elderly patients hospitalized in short-stay and rehabilitation care units suggests tentative recommendations for protein and energy intake for such patients.

In the group of 36 elderly hospitalized patients studied, the ratio of energy intake to REE influenced protein requirements; the minimal energy intake necessary to sustain a neutral nitrogen balance was 1.31 times REE (25 kcal/kg per day when 0.99 g/kg per day protein is consumed). In healthy subjects, a neutral or positive nitrogen balance can only be attained if energy intake is sufficiently high.[19]

Protein intake required to maintain a neutral nitrogen balance was 1.06 ± 0.28 g/kg per day. This finding differs considerably from the recommendation of the 1985 joint FAO/WHO/UNU report,[1] which indicates a minimal protein intake of 0.80 g/kg per day based on a study conducted on people of various ages, all of whom were in reasonably good health, but several authors have suggested that elderly people and patients in intensive care units may require a much higher protein intake.[3,9,10]

The classical way of estimating the mean protein requirement is to gradually increase protein intake until neutral nitrogen balance is reached. This method requires several periods with different protein intake, assuming that volunteers or patients are in a stable condition. Data are then used to estimate mean protein intake (in g/kg body weight per day). To be sure that 95% of the population is in neutral or positive nitrogen balance, this mean plus 2 SDs (or 25%) is calculated and defines safe protein intake.

In the patients studied here, this method could not be used, because disease was a temporary status that precluded repetition of the study with different intakes. It was therefore decided to measure nitrogen balance in conditions of spontaneous and ad libitum food intake. The regression approach has already been used in healthy individuals (see [9]).

The method used here provides an adequate estimate of mean protein intake to reach a positive nitrogen balance. In the studies reviewed previously,[9] most subjects were in positive nitrogen balance with 1 g protein/kg per day, the intake observed here. Lower intakes of protein lead to a negative protein balance, with an adaptive response tending to restore nitrogen balance. One strength of the present survey was that it studied a group in which some patients were in negative nitrogen balance despite an intake of 0.8 g/kg per day. Therefore, the status quo ante that would lead to the recommended 0.8 g/kg per day would be unethical, because it is likely that many patients would be in negative nitrogen balance.

Safe protein intake is difficult to establish in this population. The standard errors around the mean values calculated here (0.28, which is the standard deviation (SD) of the intercept, or 0.33, which also accounts for the SD of the slope and some degree of covariance between slope and intercept) may be considered wide ($\sim$ 30% of the mean value). Following the method used by the 1985 joint FAO/WHO/UNU report,[1] the classical mean plus 2 SDs may therefore appear to be inflated. The protein intake that would be adequate to ensure that 95% of older rehabilitation patients remain in positive nitrogen balance would be estimated to be 1.60 g/kg per day, similar for men and women. This large SD may stem from the small number of subjects (n = 36), although in the experiments listed in[9], the corresponding number of volunteers was sometimes much smaller. Another alternative is to use the +25% figure used previously.[9] Doing so, safe protein intake would be 1.325 g/kg per day. Yet another approach is to use the group mean values as the primary data to assess nitrogen balance (0.99 ± 0.24). Then safe protein intake would be $0.99 + 2 \times 0.24 = 1.47$ g/kg per day. Therefore, safe protein intake could be between 1.3 and 1.6 g/kg per day. Because there is no proof that a high intake is safe, 1.6 g/kg per day is not recommended. Furthermore, this higher value of safe protein intake was to be considered adequate, and because 95% of the patients had a protein intake lower than 1.47 g/kg per day (mean+2 SDs), specific means of supplying additional amounts of protein would have to be considered. Indeed, most of the elderly hospitalized patients observed seemed physically unable to increase their consumption.

A disadvantage of the study is the small number of patients; although 110 patients had been recruited initially, most had to be excluded because of incomplete data, and only 36 patients were finally retained. The study is nevertheless unique.

The REE measurements, made 5 days after hospitalization, when the patients were clinically stable, may be considered fairly precise. Similarly, protein intake, determined over a 3-day period for all patients by the same technician, may be estimated to be reasonably accurate. In contrast, nitrogen balance is likely to have been slightly overestimated, because the data used for fecal nitrogen excretion were obtained from healthy elderly individuals. Lower nitrogen balances would lead to a greater intercept along the X-axis (Figure 1) and hence a higher requirement. In calculating these figures, it was assumed that a steady-state protein intake had been prevailing for 4 to 5 days, which is the minimum for a new equilibrium to be reached after a change in intake. Because it is likely that patients were ill and food restricted before admission, and because a stable clinical state was attained before the measurements started, it is likely that patients had reached the required new equilibrium. The 1.06 g/kg per day appears therefore to be a conservative value.

It was not shown that the inflammatory status of the elderly hospitalized patients influenced nitrogen balance. This could be due to lack of power of the test or the potential plasma CRP peak might have been missed, because plasma CRP level was assessed 4 or 5 days after admission. Several patients suffered from multiple pathologies, so it was not feasible to determine the effect of initial diagnosis on nitrogen balance.

The net balance calculated here is a gross estimate that does not take into account protein traffic between organs. Indeed, infections increase protein catabolism and divert amino acids to the synthesis of acute-phase proteins in the liver and proteins for the immune system.[14] During inflammation and healing, the breakdown of muscle protein supplies amino acids to injured tissues and immune cells. Future studies should therefore target the effect of nitrogen balance on improvement of specific functions, such as healing and immune response.

Covariance analysis has shown that protein and energy intake influence nitrogen balance. Here, at a mean 0.99 g/kg per day protein intake, a neutral nitrogen balance would require a minimal energy intake equivalent to 1.31 times REE. This illustrates a novel concept of energy requirement. Indeed, the 1985 joint FAO/WHO/UNU report[1] merely defines energy requirements in healthy subjects as the amount of energy needed to maintain body weight and composition, as well as long-term good health and desirable social and economic status. In hospitalized patients, extra energy is considered to be necessary to optimize various body functions such as immune function, healing, and autonomy.[16] If nitrogen balance reflects some kind of functional status, then no less than 1.31 times REE is required. Further investigation will be needed to show to what extent greater protein and energy intake improve the functional status of elderly hospitalized patients.

In conclusion, this study indicates that elderly hospitalized patients require a minimal protein input of 1.06 g/kg per day, associated with an energy input of 1.3 times REE (25 kcal/kg per day) to be in neutral nitrogen balance. Safe protein intake is difficult to establish and may be 1.3 g/kg of body weight per day or higher (much higher than for healthy people).

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Author Contributions: C. Gaillard, E. Alix, and P. Ritz collected and analyzed the data and wrote the manuscript. G. Berrut and Y. Boirie significantly contributed to the interpretation of the data and the discussion of the manuscript.

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