POPULATIONS AT RISK

Protein-energy Undernutrition and Life-threatening Complications Among the Hospitalized Elderly

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OBJECTIVE: To determine whether elderly patients with protein-energy undernutrition at admission are at increased risk for subsequent life-threatening events after controlling for illness severity.

DESIGN: Prospective cohort study.

SETTING: University-affiliated Department of Veterans Affairs hospital.

PATIENTS: Five hundred eighty-six nonterminal patients (mean age 74 ± 6 [SD] years, 98% male, 86% white) with a length of stay of 3 days or more.

MAIN OUTCOME MEASURES: Life-threatening complications.

RESULTS: Subsequent to admission, 37 subjects (6.3%) experienced at least 1 life-threatening complication. All of the putative nutrition variables examined and many non-nutrition, illness severity measures were strongly correlated with the risk of a life-threatening complication by univariate analyses ($P < .05$ for all analyses). After controlling for illness severity, admission serum albumin, prealbumin, and cholesterol were no longer significantly correlated with the outcome. In contrast, weight loss ($>5\%$ within 6 months), body mass index, mid-arm circumference, and suprailiac skinfold thickness remained strong independent predictors. The adjusted relative risk of a life-threatening complication ranged from 2.9 (95% confidence interval [CI], 1.3 to 6.4) for a body mass index $<22 \text{ kg/m}^2$ to 7.1 (95% CI, 2.0 to 25.7) for a suprailiac skinfold thickness in the lower tertile for the study population. The putative nutrition and illness severity variables were highly intercorrelated.

CONCLUSIONS: There is a complex interrelationship between nutritional status, illness severity, and clinical outcomes among the hospitalized elderly. The serum secretory proteins and cholesterol are correlated with other indicators of illness severity and adverse outcomes, but may not be good markers of nutritional risk. In contrast, weight loss, a low body mass index, and other indicators of lean and fat mass depletion

appear to place the patient at increased risk for adverse outcomes independent of illness severity. Whether it is possible to reverse such established nutritional deficits and reduce complication risk in the acute care setting remains to be determined.

KEY WORDS: elderly; undernutrition; hospitalized; complications; protein-energy malnutrition; nutritional status; outcome assessment; health status.

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Several observational studies of elderly hospitalized patients have identified strong correlations between specific clinical markers of protein-energy nutritional status and the risk of subsequent in-hospital morbid events.¹⁻⁵ The correlations have been strongest for the serum secretory proteins and cholesterol, weight loss, and indices of body composition.¹⁻⁵ When overweight individuals are excluded from the analyses, the relationships are linear: the more severe the protein and energy deficits (as defined by the putative nutritional parameters), the greater the risk of subsequent morbidity.¹⁻⁵

These observational studies suggest that protein-energy undernutrition (PEU) is an important, potentially modifiable risk factor for poor clinical outcomes among the hospitalized elderly. However, direct evidence from appropriately designed nutrition intervention studies is lacking. In fact, as several recent reviews have pointed out,⁶⁻⁹ there is little convincing evidence that any form of nutrition intervention significantly reduces the risk of in-hospital morbidity in any age group of patients. The few studies that specifically targeted the elderly have yielded inconsistent results.¹⁰⁻¹⁴ The reason for the apparent discrepancy between the findings from the observational studies and intervention trials is not readily apparent. For some elderly patients, undernutrition (or an abnormal putative nutrition indicator) may be simply a marker for illness severity, nutritional deficits may not be easily reversed within the short time frame of hospitalization, or factors other than undernutrition may be more powerful determinants of short-term in-hospital outcomes. In addition, nutritional support may be beneficial for only select subgroups of elderly patients who do not have such powerful competing risks. Given the expense, patient discomfort, and morbidity associated with the use of various forms of nutrition support,^{15,16} it is important to

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distinguish those patients that should be targeted for nutrient interventions.

To investigate the interrelationship between nutritional status, illness severity, and clinical outcomes, we conducted a prospective study of nonterminally ill elderly patients admitted to an acute care hospital. The specific objective was to determine whether elderly patients who are protein-energy undernourished at admission are at increased risk for subsequent life-threatening adverse clinical events during hospitalization and whether the association between PEU and risk remains significant after controlling for diagnoses, functional status, and other indicators of illness severity.

METHODS

Participants

During a 3-year interval, all geriatric admissions to a general medical or surgical ward of a university-affiliated Department of Veterans Affairs Hospital were screened to determine study eligibility. Screening took place within 12 hours of admission and consisted of a complete review of the patient's current and past medical records. All patients admitted to these wards who were 65 years of age or older and free of metastatic cancer or other terminal conditions (as indicated by palliative care status) were assigned a random number. To keep study admissions in the targeted range of 3 to 4 patients per week, only patients that were assigned a random number below a pre-established cut-off were asked to enter the study. Of the 722 patients selected for study entry, 31 declined to participate. Each of the remaining 691 participants received oral and written explanations of the nature of the study and the possible risk involved prior to signing an informed consent in accordance with the ethical standards of the U.S. Department of Veterans Affairs and the Human Research Advisory Committee of the University of Arkansas for Medical Sciences. To eliminate patients with inadequate risk exposure (see definition of complication below), the 105 patients whose lengths of stay were less than 3 days were dropped from the analysis, leaving a final study sample of 586 patients.

In-hospital Evaluation

An initial assessment was completed within 48 hours of admission that included: 1) a concise social, nutritional, and functional status history obtained by a standardized series of questionnaires administered by a research assistant to each patient or the primary caregiver (if the patient was unable to answer); 2) a complete list of all primary and secondary diagnoses as recorded in the current hospital chart and old medical records; 3) a complete clinical and laboratory nutritional assessment; 4) the Mini-Mental State Exam¹⁷; 5) a detailed evaluation of functional status; and 6) an array of additional illness severity measures including hematocrit, white blood cell

count, blood urea nitrogen, total APACHE score,¹⁸ calculated diagnosis-related group length of stay, and the Charlson Weighted Index of Comorbidity.¹⁹ The variables obtained from all assessments were chosen on the basis of their ease of measurement and the results of previous studies that demonstrated their predictive importance in elderly populations.¹⁸⁻²⁶

The nutritional assessment included weight change in the prior year, suprailiac skinfold thickness, body mass index (BMI), mid-arm circumference, and serum albumin, prealbumin, and cholesterol concentrations. Previous hospital and clinic records were reviewed to document prior weights. Only weights obtained while the patient appeared to be euvoletic were recorded. Patients were not considered to be reliable sources of information regarding their own weight history. Anthropometric measurements were obtained by trained research assistants using a standardized protocol.²⁷ All blood work was obtained at admission.

Functional status was assessed using the Katz Index of Activities of Daily Living (ADL) scale,²⁸ the Philadelphia Geriatric Center Instrumental ADL Scale,²⁹ and a measure of walking endurance. The Katz ADL scale measures the level of functional independence in 6 categories: bathing, dressing, toileting, transfers, continence, and feeding.²⁸ Each category was scored on a 3-level scale with each item assigned points according to a defined decision rule (0 = independent, 1 = human help, 2 = totally dependent). Total score, obtained by adding the 6 categories, ranged from 0 (independent) to 12 (totally dependent). Because of the ceiling effect of the Katz ADL scale in the study population, a measure of walking endurance was included as part of the functional assessment. Walking endurance was an untimed assessment of the distance a subject could walk indoors with scores ranging from 0 (walks >50 yards) to 8 (unable to walk at least 3 feet).

Monitoring the Frequency of In-hospital Life-threatening Complications

On a daily basis subsequent to their admission and while they were still hospitalized, each patient's chart was reviewed and the ward team in charge of his care was interviewed to determine whether the patient developed any life-threatening complications. Patients were examined as needed to confirm or clarify data obtained from charts. Only problems that developed after the second day of hospitalization were considered complications. The initial screening of charts was completed each day by a study nurse. Any possible complications were reviewed by a physician-investigator (DHS). The reviewer was not aware of the nutrition data collected by the study. However, some nutrition data were occasionally presented in the clinicians' notes.

To avoid subjective observer bias, each postadmission complication was defined before the start of the study using rigid objective criteria developed in a previous outcome study.³⁰ The definitions of those complications that were

identified during this study are listed in Appendix A. Utilizing a method devised by Buzby et al.,³¹ a problem was defined as life-threatening on the basis of clinical criteria including a dramatic deterioration in the patient's clinical status and the need for immediate intervention, or the transfer to an intensive care unit for monitoring and treatment of a myocardial infarction. In a prior study, the instrument was found to have construct- and criterion-related validity.³² On the basis of a random sample of over 450 patients admitted to a geriatric rehabilitation service, 72% of the patients classified as having a life-threatening complication eventually died prior to leaving the hospital. The survivors had longer lengths of hospitalizations (acute plus subacute days) compared to the subjects that did not experience a life-threatening complication (100 vs 34 days; $P < .005$).

Statistical Analyses

For all analyses, the outcome variable was dichotomized (i.e., no vs 1 or more life-threatening complications). The relationship between the database variables (as independent variables) and the dichotomized outcome variable (as the dependent variable) was then analyzed using both univariate and multivariable (logistic regression) statistical techniques. There was little missing data (<1%). There was no difference in any of the analyses whether we imputed the values or left them as missing.

The first group of analyses examined the strength of the relationship between each database (nutrition and non-nutrition) variable and the dichotomized outcome variable using univariate statistics (i.e., Student's t test for comparing means and the χ^2 test for categorical parameters). Parameters that were highly skewed were appropriately transformed (e.g., log-transformed).

There is no uniformly agreed upon definition of PEU. As advocated by others, we considered the putative nutrition assessment variables to be indicators of nutrition risk. For each of these variables, values were initially categorized as signifying a high, medium, or low nutrition risk. This was done by creating 2 dummy variables for each of the nutrition variables, the first to indicate whether the measured value signified a high nutrition risk, and the second to indicate medium risk. Since appropriate population norms were not available for the anthropometric measurements, suprailiac skinfold thickness and a mid-arm circumference were categorized by study population tertiles. The risk categories for the other nutrition variables were based on prior studies.^{33,34} The subsequent univariate analyses indicated that this classification scheme could be simplified. Other than for the anthropometric measures, each nutrition assessment variable could be dichotomized (i.e., we used only 1 dummy variable). Combining the low- and medium-risk categories of the variable did not result in any loss of the variable's discriminating power. The cutoff points used to define each nutrition risk category for each variable are presented in the results section.

Diagnoses were analyzed from 2 perspectives—either as the presence or absence of an active problem in any of 22 different diagnostic categories or as the number of high-risk chronic debilitating diseases (from 0 to 7) from the following categories: congestive heart failure, non-insulin-dependent diabetes mellitus, cerebral vascular accident, dementia (Alzheimer's or multi-infarct), Parkinson's, chronic obstructive pulmonary disease, and end stage renal failure. Because of the number of non-nutrition variables included in the database, only those showing a significant association with the outcome ($P < .05$) were entered into the multivariable analyses. The non-nutrition variables were utilized in these analyses as indicators of illness severity.

Because the period of time at risk due to the length of stay was not the same for all study patients, it was possible that the variability in the risk of developing a complication could be partially or fully attributed to the variance in the length of time under observation. To exclude this possibility, it was important to determine whether the "period of time at risk" was greater for the patients who developed at least 1 life-threatening complication compared to those who had none. To make this assessment, if the patient had a life-threatening complication, "period of time at risk" was set equal to the time from hospital admission until the first complication. For patients who did not develop a complication, "period of time at risk" was set equal to the time from admission until hospital discharge. The "period of time at risk" was compared for the complication group and the no-complication group.

Multivariable Analyses

To determine if any putative nutrition variables remained significantly associated with the outcome after controlling for illness severity at admission, a series of multivariable analyses were performed. The non-nutrition variables utilized to control for illness severity in the multivariable analyses were identified first. Initially, only the preselected non-nutrition variables were included in a logistic regression analysis. A stepwise procedure was utilized to determine which variables entered the model. A second analysis was then performed that included all of the preselected variables (i.e., both the preselected non-nutrition and nutrition variables). Any non-nutrition variable that entered into either model was retained for use in subsequent analyses as an illness severity indicator. To assess whether the inclusion of the nutrition variables resulted in an improvement in predictive accuracy, the overall c-statistic from each model was compared.

Since nutrition variables are often highly intercorrelated, it was anticipated that they would compete with each other for entry into a multivariable model. For this reason, we felt that it was important to conduct an additional series of analyses in which each nutrition variable was analyzed separately from the others. For each nutrition variable, multiple analyses were run. Each analysis included

different illness severity indicator variables as covariates in the model. The purpose of these analyses was to determine the extent to which the illness severity variables confounded the association between the given nutrition variable and the outcome.

RESULTS

Population Characteristics

A general description of the study population is provided in Table 1. The active problems (i.e., clinical diagnoses) that were most prevalent within the study population at the time of admission are listed in Table 2. As shown, the majority of the subjects were very frail white males with multiple comorbid conditions. A majority (64%) had been hospitalized at least once in the previous 2 years (median of 1 prior hospital admissions, interquartile range 0 to 3), and 74% had at least 1 high-risk chronic debilitating disease (as defined above).

Subsequent to admission, 37 subjects (6.3%) experienced at least 1 life-threatening complication. The fre-

Table 1. Description of Study Population

Variables	Value (N = 586)
Mean age, y (SD)	73.6 (5.7)
Mean education, y (SD)	10.2 (3.7)
Household income, \$ (%)	
0 – <10,000	234 (40)
10 – <20,000	240 (41)
20 – <40,000	100 (17)
≥40,000	12 (2)
Married, n (%)	387 (66)
Katz Index of ADL score,* median (IQR)	0 (0 to 2)
Prescription medications, median (IQR)	6 (4 to 9)
Total medications, median (IQR)	9 (6 to 12)
Problems,† median (IQR)	
Inactive problems	5 (4 to 8)
Active problems	
Stable problems	5 (3 to 7)
Current problems	3 (2 to 5)
Unstable problems	0 (0 to 0)
Mean Mini Mental State Exam score (SD)	23.7 (6.4)
Admitted from, n (%)	
Home	512 (87.4)
Nursing home	37 (6.3)
Other hospital	37 (6.3)
White race, n (%)	498 (85)
Male gender, n (%)	574 (98)

* As described in the text, Katz Index of Activities of Daily Living (ADL) scale ranges from 0 (completely independent in bathing, dressing, toileting, transfers, continence, and feeding) to 12 (totally dependent in all categories).

† Problems were grouped into 2 categories, inactive and active. Inactive problems are defined as no longer requiring any form of treatment and having no residual effect on physical function. Active problems are defined as stable (i.e., under control with therapies provided prior to admission), current (i.e., requiring change in therapy during hospitalization), and unstable (i.e., a life-threatening condition).

IQR, interquartile range.

Table 2. Most Common Active Admission Clinical Diagnoses*

Diagnosis	N (%)†
Anemia	170 (29)
Arrhythmia	146 (25)
Arthritis	270 (46)
Benign prostatic hypertrophy	135 (23)
Coronary artery disease	275 (47)
Congestive heart failure	147 (25)
Chronic obstructive pulmonary disease	252 (43)
Diabetes	141 (24)
Gastrointestinal disease	246 (42)
Hernia	117 (20)
Hypertension	322 (55)
Tobacco abuse	146 (25)
Renal electrolyte disorder	146 (25)

* Includes primary and secondary diagnoses (i.e., active problems).

† Percent of patients with at least 1 condition from the given diagnostic category.

quency with which each complication developed and the associated outcomes are listed in Table 3. As indicated, 15 of the subjects (41%) who developed a life-threatening complication eventually died or suffered a cardiac arrest.

Predictors of a Life-threatening Complication

As shown in Table 4, all of the putative nutrition variables were highly associated with life-threatening complication risk by univariate analysis. The non-nutrition admission assessment variables that were associated with life-threatening complication risk are shown in Table 5. Age, gender, education, hemoglobin, white blood cell count, pre-admission Katz Index of ADL score, history of alcohol abuse, marital status, tobacco use, Mini Mental State Exam score, admitted from nursing home, and race were not significantly associated with the outcome.

Period of Time at Risk

The period of time at risk (i.e., the time from admission to first event [complication or discharge]) was not significantly greater for the group that developed complications compared to the subjects who experienced no complications (median [interquartile range], 7 [4 to 13] vs 7 [4 to 11] days, respectively; $P = .96$). That is to say, subjects who developed 1 or more life-threatening complications experienced their first complication a median of 7 days after admission. Subjects who never developed a complication remained in the hospital, "at risk" for a median of 7 days after admission. In contrast, the median length of stay of the complication group was much longer than that of the remaining subjects (median [interquartile range], 16 [11 to 36] vs 7 [4 to 11] days, respectively; $P < .001$).

Multivariable Models

When all 20 non-nutrition variables were entered into a stepwise logistic regression analysis, the best predictor of

Table 3. Frequency of Occurrence of Each Life-threatening Complication

Complication	Subjects, <i>n</i>	Associated Outcome
Cardiovascular		
Unstable arrhythmia	4	One subsequently had cardiac arrest.
Cardiopulmonary arrest	8	Five died during the hospitalization.
CHF	6	Two died during the hospitalization.
Myocardial infarction	3	One subsequently died.
Pulmonary		
Pneumonia	3	Two died and the other developed respiratory failure.
Respiratory failure	11	Six subsequently died.
Infectious		
Sepsis	9	Six eventually died or had a cardiac arrest.
Miscellaneous		
Death	12	Includes one subject who did not meet definition for another complication.
Shock (noncardiopulmonary)	1	Treated for anaphylaxis with eventual full recovery.
Surgical complications		
Wound dehiscence	1	Subject fully recovered.
Postoperative hemorrhage	6	Four subsequently had cardiac arrest.
Bowel necrosis	1	Treated surgically with eventual full recovery.

CHF, congestive heart failure with pulmonary edema.

which patients would subsequently develop at least 1 life-threatening in-hospital complication was the APACHE II score followed by the number of active problems at admission, diagnosis of Parkinson's disease, diagnosis of insulin-requiring diabetes, and admitted emergently (as opposed to urgent or elective admission). When all 5 of these variables were included in the logistic regression analysis, the final model was highly significant by the

$-2\text{Log Likelihood } \chi^2$ goodness-of-fit criterion (χ^2 of 54.2 with 5 *df*; $P < .001$). The model c-statistic was 0.801.

When all of the pre-selected variables (i.e., both the non-nutrition and nutrition variables from Tables 4 and 5, respectively) were entered into a stepwise logistic regression analysis, the results were very similar. The first variable to enter the model was the APACHE II score. The only nutrition variable to enter the model, lowest tertile

Table 4. Relationship Between Nutrition Risk and Life-threatening Complications

Nutrition Variable	Nutrition Risk Category	<i>n</i>	With Complications, <i>n</i> (%)	<i>P</i> Value*
Mid-arm circumference [†]				
<286 mm	High	188	26 (13.8)	
286–323 mm	Medium	213	5 (2.4)	
>323 mm	Low	185	6 (3.2)	<.001
Suprailiac skinfold [†]				
<14 mm	High	183	25 (13.7)	
14–23 mm	Medium	210	9 (4.3)	
>23 mm	Low	193	3 (1.6)	<.001
Weight loss of 5%				
Yes	High	74	14 (19.0)	
No	Low	512	23 (4.5)	<.001
Serum albumin				
<30 g/L	High	75	10 (13.3)	
≥30 g/L	Low	511	27 (5.3)	.018
Serum cholesterol				
<160 mg/dL	High	169	16 (9.5)	
≥160 mg/dL	Low	417	21 (5.0)	.046
Pre-albumin				
<18 mg/L	High	172	18 (10.5)	
≥18 mg/L	Low	414	19 (4.6)	.008
Body mass index				
<22 kg/M ²	High	117	18 (15.4)	
≥22 kg/M ²	Low	469	19 (4.0)	<.001

* *P* value based on χ^2 statistic or Fisher's Exact Test.

[†] Grouped according to tertile.

Table 5. Non-nutrition Variables That Are Significantly Associated With Complication Risk

Variable	Complication, (N = 37)	No Complication, (N = 549)	P Value
Katz Index of ADL score,* median (IQR)	2 (0 to 8)	0 (0 to 2)	<.001
Independent in 1 or more ADLs, [†] n (%)	22 (59.5)	459 (84)	<.001
Walking ability, median (IQR)	2 (0 to 12)	0 (0 to 2)	<.001
Walking endurance, median (IQR)	6 (2 to 20)	2 (0 to 6)	<.001
IADLs, median (IQR)	4 (1 to 8)	0 (0 to 4)	<.001
Chronic diseases, [‡] median (IQR)	2 (1 to 3)	1 (0 to 2)	<.001
Prescription medications, mean (SD)	8 (3.8)	6.4 (3.7)	.010
Total number medications, mean (SD)	11.1 (4.8)	9.4 (4.2)	.018
Active problems, median (IQR)	5 (3 to 7)	3 (2 to 5)	<.001
Emergency admission, n (%)	22 (59.5)	152 (27.7)	<.001
Diagnosis of			
Pneumonia, n (%)	8 (21.6)	46 (8.4)	.014
Depression, n (%)	8 (21.6)	59 (10.8)	.050
Parkinson's Disease, n (%)	3 (8.1)	6 (1.1)	.015
Insulin-requiring DM, n (%)	7 (18.9)	35 (6.4)	.012
APACHE II score, mean (SD)	14.5 (5)	10.2 (3.9)	<.001
Charlson's Co-morbidity Index, median (IQR)	3 (2 to 4)	2 (1 to 3)	<.001
Admitted to surgical service, n (%)	11 (29.7)	258 (47)	.041

* As described in the text, Katz Index of Activities of Daily Living (ADL) scale ranges from 0 (completely independent in bathing, dressing, toileting, transfers, continence, and feeding) to 12 (totally dependent in all categories).

[†] Highest level of function within the 30 days prior to admission as determined by questionnaire using either the Katz Index of ADL scale²⁸ or the Philadelphia Geriatric Center Instrumental ADL Scale.²⁹

[‡] The number of diagnoses (from 0 to 7) from the following categories: congestive heart failure, non-insulin-dependent diabetes mellitus (DM), cerebral vascular accident, dementia (Alzheimer's or multi-infarct), Parkinson's, chronic obstructive pulmonary disease, and end stage renal failure.

IQR, interquartile range.

mid-arm circumference (<286 mm), came in second followed by the number of active problems at admission, diagnosis of insulin-requiring diabetes, admitted emergently, and admitted to a surgical ward. When these 6 variables were included in the logistic regression analysis, the final model was highly significant by the $-2\text{Log Likelihood } \chi^2$ goodness-of-fit criterion (χ^2 of 70.8 with 6 df; $P < .001$). The model c-statistic was 0.836.

There were statistically significant associations between all of the nutrition and illness severity variables examined ($P < .01$ for each comparison). However, the nutrition variables differed from one another as to whether they were strong independent predictors of a life-threatening complication. This is demonstrated in Table 6. After controlling for 1 or more of the illness severity indicators, the serum secretory proteins and cholesterol were no longer significantly associated with the outcome. The relationship between each of the remaining 4 nutrition indicators and the outcome also changed after controlling for the non-nutrition health status indicators. However, these 4 nutrition indicators, BMI, mid-arm circumference, suprailiac skinfold thickness, and significant weight loss, remained strongly associated with the outcome.

DISCUSSION

Consistent with prior studies, this investigation demonstrates that there is a strong association between specific putative markers of protein-energy nutritional

status and the risk of subsequent life-threatening adverse events in the targeted population of nonterminally ill hospitalized elderly patients. This indicates that undernourished elderly patients are at increased risk of adverse outcomes. It remains uncertain as to whether the nutritional deficits can be corrected or outcomes improved through any form of nutritional therapies. The failure of prior intervention studies to demonstrate that nutrition support improves clinical outcomes suggests that the course of certain diseases may not be strongly influenced by the patient's nutrient intake.⁶⁻⁹ Loss of appetite and PEU may develop as a consequence of the disease. The severity of the nutritional deficits may be significant only as a marker of illness severity. However, this study provides evidence to suggest that there may be alternate explanations as to why nutrition intervention trials have generally not shown beneficial results.

In addition to the nutritional markers, many non-nutritional markers of health status were identified to be powerful risk indicators. When both the nutritional and non-nutritional variables were included in the multivariable analysis, mid-arm circumference was the only nutrition variable to enter the model. BMI, suprailiac skinfold thickness, and greater than 5% weight loss in 6 months were comparable substitutes for mid-arm circumference. These 4 variables are all measures of body composition. Low values generally reflect chronic states of nutritional deprivation that include a depletion of energy reserves and/or lean body mass. To reduce the risk of nutrition-related

Table 6. The Relationship Between Each Nutrition Variable and the Outcome After Controlling for Selected Non-nutrition Variables*

Nutrition Variable	Unadjusted Relative Risk (95% CI)	Adjusted Relative Risk (95% CI)						Admitted to a	
		APACHE II Score	Active Problems	Insulin-requiring Diabetes	Emergency Admission	Parkinson's	Surgical Ward	All Variables	
Body mass index <22 kg/m ²	4.1 (2.1 to 8.0)	2.8 (1.4 to 5.8)	3.2 (1.6 to 6.3)	4.7 (2.4 to 9.5)	3.3 (1.7 to 6.6)	4.0 (2.0 to 8.1)	3.8 (1.9 to 7.8)	2.9 (1.3 to 6.4) [†]	
Albumin <30 g/L	2.7 (1.2 to 5.7)	1.7 (0.7 to 3.8)	1.3 (0.6 to 3.1)	2.5 (1.1 to 5.4)	2.1 (1.0 to 4.7)	2.8 (1.3 to 6.2)	2.4 (1.1 to 5.2)	1.2 (0.5 to 3.0)	
Mid-arm circumference, tertile									
Lowest (<28.6 mm)	4.1 (1.7 to 9.6)	3.0 (1.2 to 7.2)	2.9 (1.2 to 6.9)	4.6 (1.9 to 11.1)	3.6 (1.5 to 8.7)	4.7 (1.9 to 11.8)	4.4 (1.7 to 11.0)	3.3 (1.2 to 9.1) [†]	
Middle (28.6 to 32.3 mm)	0.6 (0.2 to 2.0)	0.6 (0.2 to 1.9)	0.4 (0.1 to 1.4)	0.6 (0.2 to 1.9)	0.6 (0.2 to 1.9)	0.7 (0.2 to 2.4)	0.7 (0.2 to 2.4)	0.5 (0.1 to 1.8)	
Upper (>32.3 mm)	1	1	1	1	1	1	1	1	
Suprailiac skinfold, tertile									
Lowest (<14 mm)	10.0 (3.0 to 33.6)	7.3 (2.1 to 25.0)	7.7 (2.3 to 26.4)	11.0 (3.2 to 37.5)	8.9 (2.6 to 30.3)	9.6 (2.8 to 32.6)	9.2 (2.7 to 31.2)	7.1 (2.0 to 25.7) [†]	
Middle (14 to 23 mm)	3.2 (0.9 to 11.7)	3.0 (0.8 to 11.2)	2.6 (0.7 to 9.8)	3.2 (0.9 to 11.8)	3.1 (0.8 to 11.5)	2.9 (0.8 to 10.7)	2.8 (0.7 to 10.6)	2.5 (0.6 to 9.8)	
Upper (>23 mm)	1	1	1	1	1	1	1	1	
Pre-albumin <180 mg/L	2.6 (1.3 to 5.0)	2.2 (1.1 to 4.4)	1.8 (0.9 to 3.6)	2.4 (1.2 to 4.7)	2.0 (1.0 to 3.9)	2.5 (1.3 to 5.0)	2.2 (1.1 to 4.3)	1.5 (0.7 to 3.3)	
Cholesterol <160 mg/dL	2.1 (1.1 to 4.1)	1.7 (0.8 to 3.4)	1.5 (0.8 to 3.1)	2.0 (1.0 to 4.0)	1.7 (0.9 to 3.4)	2.0 (1.0 to 3.9)	1.8 (0.9 to 3.5)	1.1 (0.5 to 2.5)	
Weight >5%	4.7 (2.3 to 9.6)	3.4 (1.6 to 7.2)	3.3 (1.6 to 7.1)	5.5 (2.7 to 11.6)	4.5 (2.2 to 9.3)	4.9 (2.4 to 10.1)	4.5 (2.1 to 9.2)	3.6 (1.5 to 8.6) [†]	

* Sample size = 586 for all models.

† Values are significant.

complications in this patient population, it is likely that strategies will need to be developed that will correct these deficits.

Undernourished, frail elderly patients are sometimes able to slowly replete their energy stores.³⁵ However, it may take several months or longer even with an optimal energy intake. If volitional nutrient intake is not adequate, supplemental feedings or other strategies to improve caloric intake would need to be implemented on a long-term basis. But even this may not be enough to improve clinical outcomes. Any lean body mass deficits and associated functional deficits would probably also need to be corrected. Increasing total protein and caloric intake does not necessarily lead to a change in lean body mass or an improvement in functional status.³⁶⁻³⁸ To correct these deficits, long-term, multi-modality interventions are probably needed. This may be one reason why nutrition intervention trials have not been successful in improving outcomes. Nearly all of these trials examined only short-term unimodality interventions. Studies are needed to determine whether combining nutrition support with other treatment modalities improves therapeutic effectiveness. The combined treatment programs might include muscle strengthening exercises and/or the use of anabolic hormones.

Unlike the indices of body composition, serum albumin, prealbumin, and cholesterol were not powerful independent predictors of life-threatening complications in this study. After adjusting for the non-nutritional health status indicators, none of these 3 variables remained significantly associated with the outcome. Although frequently used as nutrition indicators, these parameters are not specific for nutritional deprivation. A number of other conditions, particularly inflammatory disorders, can produce a decline in all three.³⁹ Serum albumin and cholesterol also lack sensitivity as nutrition indicators. Their values may not change even after several weeks of starvation in an otherwise healthy individual.^{40,41} For these reasons, there is considerable controversy as to whether these 2 variables should be used as indicators of nutritional status.³⁹ They may be better thought of as nonspecific indicators of health status or illness severity. The need for nutritional support should not be based on the serum albumin or cholesterol values.

The finding that prealbumin is not a independent risk indicator is consistent with prior studies.³⁹ In contrast to albumin and cholesterol, the serum prealbumin concentration is very sensitive to changes in both nutrient intake and disease activity. The serum concentration can decline by as much as 50% subsequent to a major physiologic insult.⁴⁰ In an otherwise healthy person, a comparable drop in the serum concentration can result after only 3 to 5 days of a very low nutrient intake.³⁹ Consequently, a low prealbumin is not necessarily indicative of serious pathology and it cannot be used to gauge the extent of any potential nutritional deficit. For this reason, prealbumin is not a good indicator of nutritional risk. It is probably better

suiting to gauge the adequacy of nutrient intake during the resolution phase of an acute illness. In such a setting, when the prealbumin concentration is low, its failure to increase by at least 20 mg/L in 1 week is considered an indication of inadequate nutrient intake or ongoing inflammation and should prompt a careful assessment of the patient and the nutrient regimen being employed.³⁹

This study included only patients who were over the age of 64, had a nonterminal condition, and remained hospitalized for more than 2 days. This was done for a specific reason. The study was developed as part of a larger, proposed series of investigations designed to identify optimal use of nutritional interventions for managing older hospitalized patients who are undernourished at admission. Only subjects with an adequate length of exposure to be at risk for developing a complication (as per the definition of a complication) were included in the study. Limiting study inclusion to patients who remained hospitalized for more than 2 days placed the focus of the study on the more complex long-term-stay patients and excluded patients who were less likely to need or benefit from nutrition support, including those admitted for uncomplicated procedures or observation and those who responded quickly to initial non-nutritional interventions. Patients who were receiving palliation for metastatic cancer or other terminal conditions also were excluded because it was assumed that aggressive use of nutrition support in this population likely would be an unwarranted stressor.

Predefined criteria were utilized to define life-threatening complications. We suspect that our definitions were highly specific but may have had only moderate sensitivity. This is suggested by the fact that one of the subjects who died did not meet another definition of a complication. We are particularly concerned that we may have missed some episodes of sepsis. During the study, several of the study subjects were treated with antibiotics on the basis of a clinical suspicion of sepsis. However, all diagnostic studies failed to identify a clear source of infection, and the subjects eventually improved. Not meeting our definition of the complication, these subjects were not listed as having sepsis. Since many older subjects do not present with classic signs or symptoms even when suffering from a potentially fatal condition, it is often not possible to make a definitive diagnosis. What impact this had on the study results is not clear.

This study demonstrates a complex interrelationship between nutritional status, disease, and outcomes among the hospitalized elderly. Failure to fully understand the complexity of this interrelationship has important clinical implications. Lacking proof of its efficacy to improve outcomes, many clinicians are reluctant to provide nutrition support to their elderly hospitalized patients even after potentially serious nutritional deficits have been identified.¹⁰ Whether a more aggressive approach to evaluating and treating nutritional deficits in this population is warranted has yet to be established. In order to

guarantee that elderly hospitalized patients receive optimal nutritional care, a greater understanding of these nutrition-related issues must be acquired.

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REFERENCES

1. Volkert D, Kruse W, Oster P, Schlierf G. Malnutrition in geriatric patients: diagnostic and prognostic significance of nutritional parameters. *Ann Nutr Metab*. 1992;36:97-112.
2. Potter JF, Schafer DF, Bohi RL. In-hospital mortality as a function of body mass index: an age-dependent variable. *J Gerontol*. 1988; 43:M59-63.
3. Constans T, Bacq Y, Brechot JF, Guilmot JL, Choutet P, Lamière F. Protein-energy malnutrition in elderly medical patients. *J Am Geriatr Soc*. 1992;40:263-8.
4. Cederholm T, Jagren C, Hellstrom K. Outcome of protein-energy malnutrition in elderly medical patients. *Am J Med*. 1995;98: 67-74.
5. Covinsky KE, Martin GE, Beyth RJ, Justice AC, Sehgal AR, Landefeld CS. The relationship between clinical assessments of nutritional status and adverse outcomes in older hospitalized medical patients. *J Am Geriatr Soc*. 1999;47:532-8.
6. Avenell A, Handoll HH. Nutritional supplementation for hip fracture aftercare in the elderly. *Cochrane Database Syst Rev*. 2000;CD001880.
7. Heyland DK, MacDonald S, Keefe L, Drover JW. Total parenteral nutrition in the critically ill patient: a meta-analysis. *JAMA*. 1998; 280:2013-19.
8. Souba WW. Nutritional support. *N Engl J Med*. 1997;336:41-8.
9. Sullivan DH. The role of nutrition in increased morbidity and mortality. *Clin Geriatr Med*. 1995;11:661-74.
10. Sullivan DH, Nelson CL, Bopp MM, Puskasich-May CL, Walls RC. Nightly enteral nutrition support of elderly hip fracture patients: a phase I trial. *J Am Coll Nutr*. 1998;17:155-61.
11. Bastow MD, Rawlings J, Allison SP. Benefits of supplementary tube feeding after fractured neck of femur: a randomized controlled trial. *BMJ*. 1983;278:1589-92.
12. Delmi M, Rapin CH, Bengoa JM, Delmas PD, Vasey H, Bonjour JP. Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet*. 1990;335:1013-6.
13. Schurch MA, Rizzoli R, Slosman D, Vadas L, Vergnaud P, Bonjour JP. Protein supplements increase serum insulin-like growth factor-I levels and attenuate proximal femur bone loss in patients with recent hip fracture. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med*. 1998;128:801-9.
14. Stableforth PG. Supplement feeds and nitrogen and calorie balance following femoral neck fracture. *Br J Surg*. 1986;73:651-5.
15. Karkeck JM. Nutrition support for the elderly. *Nutr Clin Pract*. 1993;8:211-9.
16. McCamish MA. Malnutrition and nutrition support interventions: cost, benefits, and outcomes. *Nutrition*. 1993;9:556-7.
17. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-98.
18. Lockrem JD, Lopez E, Gallagher J, Church GE, Estafanous FG. Severity of illness: APACHE II analysis of an ICU population. *Cleve Clin J Med*. 1991;58:477-86.

19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-83.
20. Agarwal N, Acevedo F, Leighton LS, Cayten CG, Pitchumoni CS. Predictive ability of various nutritional variables for mortality in elderly people. *Am J Clin Nutr.* 1988;48:1173-8.
21. Narain P, Rubenstein LZ, Wieland GD, et al. Predictors of immediate and 6-month outcomes in hospitalized elderly patients: the importance of functional status. *J Am Geriatr Soc.* 1988;36:775-83.
22. Epstein AM, Stern RS, Tognetti J, Begg CB, Hartley RM, Cumella E Jr. The association of patients' socioeconomic characteristics with the length of hospital stay and hospital charges within diagnosis-related groups. *N Engl J Med.* 1988;318:1579-85.
23. Iezzoni LI, Ash AS, Coffman GA, Moskowitz MA. Predicting in-hospital mortality. A comparison of severity measurement approaches. *Med Care.* 1992;30:347-59.
24. Green J, Passman LJ, Wintfeld N. Analyzing hospital mortality. The consequences of diversity in patient mix. *JAMA.* 1991;265:1849-53.
25. Cohen HJ, Saltz CC, Samsa G, McVey L, Davis D, Feussner JR. Predictors of two-year post-hospitalization mortality among elderly veterans in a study evaluating a geriatric consultation team. *J Am Geriatr Soc.* 1992;40:1231-5.
26. Pompei P, Charlson ME, Ales K, MacKenzie CR, Norton M. Relating patient characteristics at the time of admission to outcomes of hospitalization. *J Clin Epidemiol.* 1991;44:1063-9.
27. Sullivan DH, Patch GA, Baden AL, Lipschitz DA. An approach to assessing the reliability of anthropometrics in elderly patients. *J Am Geriatr Soc.* 1989;37:607-13.
28. Katz S, Ford AB, Moskowitz RW, Jackson BA, Joffee MW, Cleveland MA. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA.* 1963;185:914-9.
29. Lawton MP. Assessing the competence of older people. In: Kent D, Kastenbaum R, Sherwood S, eds. *Research Planning and Action for the Elderly.* New York: Behavioral Publications; 1972: 123-45.
30. Sullivan DH, Patch GA, Walls RC, Lipschitz DA. Impact of nutritional status on morbidity and mortality in a select population of geriatric rehabilitation patients. *Am J Clin Nutr.* 1990;51:749-58.
31. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg.* 1980;139:160-7.
32. Sullivan DH, Walls RC. The risk of life-threatening complications in a select population of geriatric patients: the impact of nutritional status. *J Am Coll Nutr.* 1995;14:29-36.
33. Landi F, Zuccala G, Gambassi G, et al. Body mass index and mortality among older people living in the community. *J Am Geriatr Soc.* 1999;47:1072-76.
34. Rudman D, Mattson DE, Nagraj HS, et al. Prognostic significance of serum cholesterol in nursing home men. *J Parenter Enteral Nutr.* 1988;12:155-58.
35. Hebuterne X, Broussard JF, Rampal P. Acute renutrition by cyclic enteral nutrition in elderly and younger patients. *JAMA.* 1995;273:638-43.
36. Campbell IT. Assessing the efficacy of nutritional support. *Baillieres Clin Endocrinol Metab.* 1997;11:753-69.
37. Watters JM, Kirkpatrick SM, Norris SB, Shamji FM, Wells GA. Immediate postoperative enteral feeding results in impaired respiratory mechanics and decreased mobility. *Ann Surg.* 1997;226:369-77.
38. Whittaker JS, Ryan CF, Buckley PA, Road JD. The effects of refeeding on peripheral and respiratory muscle function in malnourished chronic obstructive pulmonary disease patients. *Am Rev Respir Dis.* 1990;142:283-88.
39. Sullivan DH. What do the serum proteins tell us about our elderly patients? *J Gerontol A Biol Sci Med Sci.* 2001;56:M71-4.
40. Spiekerman AM. Proteins used in nutritional assessment. *Clin Lab Med.* 1993;13:353-69.
41. Forse RA, Shizgal HM. Serum albumin and nutritional status. *J Parenter Enteral Nutr.* 1980;4:450-4.

APPENDIX A

Definitions of Life-threatening Complications

Cardiovascular

Unstable arrhythmia: EKG documentation of atrial fibrillation or flutter with rapid ventricular response resulting in hypotension or need for immediate cardioversion

Cardiopulmonary arrest: loss of pulse and blood pressure with EKG documentation of ventricular fibrillation, electrical mechanical dissociation, or asystoli

CHF with pulmonary edema: congestive heart failure with pulmonary edema made by standard clinical and radiographic criteria including the development of respiratory failure and/or cardiogenic shock and requiring urgent treatment with diuretics, oxygen, and other agents such as vasodilators

Myocardial infarction: new Q waves (>0.03 s) in duration in 2 or more contiguous leads or a diagnostic rise in serum total creatine kinase (CK) levels (>130 U/L), with CK-MB fraction >7 ng/mL and a quotient (CK-MD/total CK) >0.04

Pulmonary

Pneumonia: pneumonia documented by an abnormal chest x-ray and treated with antibiotics with the subsequent development of respiratory failure or death

Respiratory failure: need for ventilatory assistance or $>60\%$ oxygen for more than an hour to maintain the PO_2 greater than 60 torr

Infectious

Sepsis: required a positive blood culture associated with hypotension or hypoperfusion

Miscellaneous

Death: from any cause

Shock (excluding cardiopulmonary or infectious): development of hypotension that necessitated treatment with vasopressors or volume expanders

Surgical

Wound dehiscence: complete, involving separation of all layers of the surgical wound

Postoperative hemorrhage: unexpected postoperative bleeding with associated hypotension that required 2 or more units of blood beyond what the surgeons considered to be routine blood replacement within the first 24 hours subsequent to surgery

Bowel perforation, obstruction, or necrosis: diagnosed radiographically, endoscopically, or at laparotomy