Influence of nutrition, thyroid hormones, and rectal temperature on in-hospital mortality of elderly patients with acute illness[1–4]

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ABSTRACT The present study was undertaken to investigate the interrelation of nutrition, core temperature, and thyroid function and their influence on survival of patients aged ≥70 y admitted to the hospital with acute conditions. Sixty-seven patients entered the study. Nutritional state, thyroid function, rectal temperature, and the APACHE II score were recorded at admission. The patients were followed until death or hospital discharge. Patients with a serum albumin concentration <35 g/L showed a lower triiodothyronine (T_3) concentration, a higher reverse triiodothyronine (rT_3) concentration, and a higher death rate. Prior weight loss (≥10%) did not influence thyroid status but increased the mortality rate. Eleven patients were hypothermic (<36.5 °C) and had a higher mortality, lower total T_3 concentration, and higher rT_3 concentration than the normothermic or hyperthermic subjects. Serum albumin, body weight, and total T_3 concentration were higher in survivors ($n = 51$) than in nonsurvivors ($n = 16$). Ongoing weight loss and hypoalbuminemia at admission are highly prevalent in elderly people with acute disease, and influence their clinical outcome. Mild hypothermia was a good predictor of death. Hypoalbuminemia and hypothermia were associated with low T_3 and high rT_3 values. *Am J Clin Nutr* 1995; 61:597–602

KEY WORDS Temperature, thyroid hormones, nutrition, elderly people, mortality

Introduction

The prolongation of life expectancy has led to an increasing demand for health care by elderly people. The population aged ≥70 y requires emergency hospital admission more often than does the younger population and has a higher than average in-hospital mortality for acute illness (1), probably because they are less able to cope with the physiological impact of severe disease. The difficulty by old patients in coping with acute conditions may be related to malnutrition and to their reduced ability to mount an appropriate neuroendocrine adaptive response to acute stress. Both derangements may be interrelated.

The risk of malnutrition increases with age (2–5), and nutritional state has been proven to influence clinical outcome in several settings (6–8). Old patients are at higher risk of suffering from disturbances of body temperature regulation and this may be partly related to undernutrition (9, 10) and the resulting alteration in the plasma concentration of thyroid hormones. Accidental hypothermia (rectal temperature <35 °C), usually as a result of exposure to cold temperatures, has been associated with a high mortality (8). However, mild hypothermia (rectal temperature between 35 °C and 36.5 °C) resulting from physiological inadaptation at the time of an emergency admission, has not received proper attention. In fact, it may be much more prevalent than commonly thought and may also adversely influence clinical outcome.

The aim of the present study was to investigate whether nutritional state, plasma concentration of thyroid hormones, and rectal temperature may influence in-hospital mortality in elderly patients with acute medical illness and whether a relationship exists among malnutrition, low circulating triiodothyronine concentrations, and mild hypothermia.

Patients and methods

From February 1991 to May 1992, 69 patients aged ≥70 y, consecutively admitted for acute medical conditions under the care of one of us (RN), were prospectively investigated. Excluded were patients not requiring hospital admission, with past medical history of thyroid disease, and taking thyroid replacement therapy or drugs known to influence thyroid hormone concentrations. Patients were studied and blood was sampled at the time of emergency admission before any ther-

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apeutic intervention (drugs, albumin, fluid therapy, oxygen administration, etc).

The severity of clinical presentation was assessed by the APACHE (Acute Physiologic and Chronic Health Evaluation) II score (11). Nutrition state was assessed by analyzing the following measurements: actual weight, percentage of body weight lost, triceps skinfold thickness, serum albumin, prealbumin, transferrin, and cholesterol. Triceps-skinfold-thickness values were expressed as percentiles from tables calculated for the Spanish population (12). Malnutrition was diagnosed if weight loss was ≥10% of the usual body weight or the serum albumin concentration was <35 g/L. Total thyroxine (T_4), triiodothyronine (T_3), reverse T_3 (rT_3), thyroid-binding globulin, and thyroid stimulating hormone (TSH) were determined by radioimmunoassay (Diagnostics Production Corp, Behring, Düsseldorf, Germany). Rectal temperature was measured with a newborn rectal thermometer (ICO Medical, Barcelona, Spain) with the sensor ≥8 cm from the anal verge. Hypothermia was defined as a rectal temperature <36.5 °C.

Death within the same hospital admission was considered the end point from which to calculate the sample size. The anticipated fatality rate was between 15% and 25% and the significance level (maximum probability of type I error) and power (1 minus the maximum probability of type II error) were both set at 5%. Comparison between means was assessed by two-tailed, unpaired Student's *t* test. Chi-square test or Fisher's exact test, when appropriate, were used to determine the significance when proportions were compared. Stepwise discriminant analysis was used as a multivariate method to select the subset of variables significantly related to mortality. Among multivariate techniques, discriminant analysis was chosen because the majority of potentially predictive variables were quantitative and normally distributed and the remaining were dichotomous (13).

Results

Demographics and admission data

Two patients were excluded because of subclinical hypothyroidism. Both had high TSH values (42.8 and 29.1 mU/L). Sixty-seven patients were available for analysis. There were 22 men and 45 women. The mean age was 79.2 ± 6 y (range 70–96 y) and there were no significant differences between sex groups.

Diagnoses at admission are shown in **Table 1.** Initial clinical, nutritional, and endocrine assessments are shown in **Table 2.** Malnutrition by one or two criteria was present in 38 (56%) patients: 23 (35%) patients manifested a weight loss ≥10% of their usual body weight and 29 (43%) patients had a serum albumin concentration <35 g/L. Patients with weight loss ≥10% had a lower serum albumin concentration than did those without weight loss (31.7 ± 6 vs 36 ± 5 g/L, $P = 0.004$). Low T_3 values (<0.9 nmol/L) were observed in 31 (46%) patients, and high rT_3 values were observed in 34 (51%) patients. Eleven patients (17%) had a rectal temperature <36.5 °C and were considered hypothermic in subsequent analysis.

TABLE 1
Diagnosis of the 67 patients aged ≥70 y at the time of admission

Pneumonia	17
Stroke	10
Hip fracture	5
Fluid and electrolyte disturbances	5
Congestive heart failure	5
Gastrointestinal hemorrhage	4
Arthralgia	3
Cirrhosis	2
Soft tissue infections	2
Other	15

Clinical, hormonal, and nutritional states

During the evaluation period, 19 patients (28%) developed clinical complications. There were 16 (24%) deaths. Differences in clinical, hormonal, and nutritional states between survivors and nonsurvivors are outlined in **Table 3.** Both a past history of weight loss and hypoalbuminemia had a significant influence on mortality. Patients with prior weight loss had a higher mortality than did those without weight loss (40% vs 21%, $P = 0.04$) and patients with hypoalbuminemia had a higher mortality than did those with a normal serum albumin concentration (37% vs 13%, $P = 0.018$).

Hypoalbuminemic patients had lower T_3 concentrations, higher TSH concentrations, and threefold the death rate of their normoalbuminemic counterparts (**Table 4**). The plasma concentration of thyroid hormones did not differ between patients with or without weight loss. Hypothermic patients had lower T_3 and T_4 and higher rT_3 plasma concentrations; a worse mean APACHE II score; and four times the death rate of the normothermic or hyperthermic patients (**Table 5**). No direct relationship could be demonstrated between anthropometric nutritional markers and rectal temperature. However, the serum albumin concentration tended to be lower in hypothermic patients (32 vs 35.3 g/L, $P = 0.1$). Patients with low T_3 concentrations had higher APACHE II scores and low albumin values, but weight, weight loss, prealbumin concentration, and rectal temperature were not significantly different (**Table 6**).

From the stepwise discriminant analysis, serum albumin concentration, rectal temperature, and rT_3 concentration emerged as the only significant predictors of mortality. The following discriminant function was obtained:

$$D = (0.78 \times \text{rectal temperature}) + 0.092 \times \text{albuminemia})$$
$$+ (0.99 \times rT_3 - 31.7)$$

The probability of mortality was obtained from such function by an expression derived from Bayes' theorem. The distribution of this probability follows a sigmoid curve (**Figure 1**). The sensitivity of this algorithm to predict mortality in the same sample was 75%, the specificity was 82%, and the overall predictive value was 81%.

Discussion

The in-hospital fatality rate among elderly patients being admitted as emergencies at our institution was 20%. The reason for this high mortality may be that elderly patients are less able to cope with acute stress due to malnutrition and inappropriate physiological adaptation.

TABLE 2
Clinical and laboratory characteristics of 67 patients aged ≥70 y at the time of admission[1]

Index	Study values	Normal range[2]
Age (y)	79.2 ± 6.1 (77.8–80.8)	
Weight (kg)	57.7 ± 12.1 (54.7–60.7)	
Loss of body weight (%)	5.8 ± 7.9 (3.9–7.8)	<5
APACHE II score	16.4 ± 3.9 (15.5–17.4)	
Tricipital skinfold thickness (percentile)	21.9 ± 17.8 (17.6–26.3)	
Serum albumin (g/L)	34.7 ± 6.2 (33.2–36.3)	35–55
Serum prealbumin (mol/L)	37.8 ± 20.3 (32.9–42.8)	30.6–72
Serum cholesterol (mmol/L)	4.8 ± 1.2 (4.5–5.1)	3.6–6.9
Serum transferrin (μmol/L)	25.8 ± 9.1 (23.6–28.1)	24.6–44.8
Thyroxine (nmol/L)	98.1 ± 25.7 (92–104)	58–161
Triiodothyronine (nmol/L)	0.98 ± 0.4 (0.9–1.1)	0.9–2.9
Thyroid stimulating hormone (mU/L)	1.4 ± 1.0 (1.2–1.7)	0.5–5
Reverse triiodothyronine (μmol/L)	10.3 ± 7.8 (8.4–12.2)	1.5–7.7

[1] $\bar{x}$ ± SD; 95% CIs in parentheses. APACHE, Acute Physiologic and Chronic Health Evaluation.
[2] Normal ranges for an adult population in the area of the study; normal ranges for tricipital skinfold thickness are dependent on age (4).

When different definition criteria were used, a high prevalence of malnutrition has been repeatedly reported in elderly people that are free-living (2, 14–16), are institutionalized (17), are general medical outpatients (3, 18, 19), are hospital inpatients because of chronic disease (2), and have a hip fracture (8, 20). According to our criteria, more than half of the patients investigated were malnourished and this had an influence on in-hospital mortality, because the death rate among malnourished subjects was two- to threefold that of well-nourished subjects. There are few reports on the nutritional state of elderly patients being admitted to hospital. Sullivan et al (17) showed that the amount of weight loss before admission was significantly lower in long-term (within 1 y) survivors than in nonsurvivors after discharge from the hospital. In a follow-up study of elderly subjects, Tayback et al (21) found that a low body mass index correlated with an increased mortality. The metabolic index with the best predictive value, however, is the serum albumin concentration. In a report on the influence of several nutritional markers on in-hospital mortality of elderly patients, Agarwal et al (7) found that the value of serum albumin remained significant even when age and diagnosis were held constant. This finding agrees with ours and suggests that serum albumin may be the simplest best single predictor of mortality, facilitating early identification of the patients at risk. Whether hypoalbuminemia should be considered of nutritional origin in the patient population investigated at our institution remains controversial because albumin synthesis may be acutely inhibited as a result of the disease itself (negative acute-phase reactant). Several facts make us feel that in our patients, hypoalbuminemia may have a nutritional component reflecting previous long-standing limitation of food intake: *1*) blood was withdrawn early in the course of the disease, before any intravenous fluid administration; *2*) anthropometric variables were worse in nonsurvivors; and *3*) patients with previous weight loss presented with significantly lower serum albumin concentration (kwashiorkor-like malnutrition). Data on

TABLE 3
Differences between survivors and nonsurvivors

Index	Survivors (n = 51)	Nonsurvivors (n = 16)
Age (y)	80 ± 6 (78–81)[1]	78 ± 6 (75–81)
Weight (kg)	60 ± 12 (56–63)	52 ± 10 (46–57)[2]
Loss of body weight (%)	4.8 ± 7.5 (2.7–7)	9.1 ± 8.3 (4.7–13.6)
APACHE II score	16 ± 4 (14.5–16.5)	19 ± 4 (17.3–21.2)[3]
Triceps skinfold thickness (percentile)	24 ± 18 (19–29)	15 ± 14 (8–23)
Serum albumin (g/L)	35.9 ± 5.9 (34.2–37.6)	31.1 ± 6.0 (33.2–36.3)[4]
Serum prealbumin (mol/L)	43 ± 30 (26.8–59.0)	36 ± 16 (31.7–40.7)
Serum cholesterol (mmol/L)	4.9 ± 1.3 (4.5–5.2)	4.6 ± 1.2 (3.9–5.2)
Serum transferrin (μmol/L)	25.5 ± 8.8 (23.1–28.1)	26.5 ± 10.4 (20.9–32.1)
Thyroxine (nmol/L)	100.6 ± 24.3 (94.2–107.1)	89 ± 28.9 (73.5–104.5)
Triiodothyronine (nmol/L)	1.1 ± 0.4 (0.9–1.2)	0.7 ± 0.3 (0.6–0.9)[4]
Thyroid stimulating hormone (mU/L)	1.4 ± 1.0 (1.1–1.7)	1.4 ± 1.0 (0.9–1.9)
Reverse triiodothyronine (μmol/L)	8.6 ± 5.4 (7.1–10.2)	15.2 ± 11.7 (9.1–21.6)[5]
Hypothermia (%)	8	46[3]
Low triiodothyronine (%)	37	75

[1] $\bar{x}$ ± SD; 95% CIs in parentheses. APACHE, Acute Physiologic and Chronic Health Evaluation.
[2–5] Significantly different from survivors: [2] P = 0.2, [3] P = 0.0005, [4] P = 0.006, [5] P = 0.002.

TABLE 4
Thyroid status among hypoalbuminemic and normoalbuminemic patients

Index	Hypoalbuminemic[1] (n = 29)	Normoalbuminemic (n = 38)
Thyroxine (nmol/L)	98 ± 28 (73.5–105.3)[2]	98 ± 23 (93.9–107.6)
Triiodothyronine (nmol/L)	0.8 ± 0.4 (0.6–0.9)	1.1 ± 0.4 (0.9–1.2)[3]
Thyroid stimulating hormone (mU/L)	1.2 ± 0.9 (0.9–1.9)	1.7 ± 1.1 (1.1–1.7)
Reverse triiodothyronine (μmol/L)	13.4 ± 9.5 (9.1–21.6)	7.9 ± 5.1 (7.1–10.2)[4]
APACHE II score[5]	17 ± 3 (16–18)	16 ± 4 (15–17)
Death rate (%)	38	13[6]

[1] Serum albumin concentration < 35 g/L.
[2] $\bar{x}$ ± SD; 95% CIs in parentheses.
[3,4,6] Significantly different from hypoalbuminemic patients: [3] $P = 0.001$, [4] $P = 0.003$, [6] $P = 0.018$.
[5] APACHE, Acute Physiologic and Chronic Health Evaluation.

previous dietary intake, however, were not available in this study.

The high mortality of malnourished elderly patients may be due to their inability to mount an appropriate neuroendocrine response to stress. It has been demonstrated that, in aged individuals, low concentrations of T_3 correlate with a quantitative measure of the severity of illness (22). The mean T_3 value in our patient population was in the low range of reference values, and that for rT_3 was above the upper limit of normal, whereas TSH was normal. Thus, overall, these patients presented with the euthyroid sick syndrome, previously described in severe nonthyroidal disease (23, 24). Furthermore, patients with low T_3 concentrations had a higher APACHE II score and low albumin concentration, suggesting a link between suboptimal thyroid status, previous nutrition, and appropriateness of the physiological response. The albumin concentration was associated with the plasma concentration of thyroid hormones. T_3 values were significantly lower in hypoalbuminemic patients and were associated with lower TSH and higher rT_3 plasma concentrations. These results are similar to those of Gaytan et al (25), who also showed low T_3 values in protein-energy malnutrition. Thus, it is not possible to ascertain whether the APACHE II score reflects the severity of the disease itself or the appropriateness of the patients' physiological response to an acute illness.

There is no evidence that low body temperature (<36.5 °C) is a common finding in the healthy geriatric population (26). Previous reports have emphasized the importance of overt, often accidental, hypothermia in the clinical outcome of acutely ill elderly patients, although this has not been considered as part of a more general physiological derangement (9, 27, 28). Unlike studies focused on severe hypothermia (core temperature <35 °C) as a primary diagnosis, in the present report hypothermia was defined as a rectal temperature <36.5 °C and was found in 11 patients, of which 7 died while in the hospital. The increased death risk of mildly hypothermic patients is also reflected by the fact that the APACHE II score was worse by four points in patients with a rectal temperature <36.5 °C. This finding reemphasizes that the APACHE II score is a good reflection of the patient's response to disease. The relationship between mild hypothermia and death was also reported by our group in patients with massive bowel infarction (29), many of whom were aged ≥70 y and by Bastow et al (8) in patients with a fractured femoral neck. In another report on thermoregulation failure in hospitalized elderly patients, the underlying conditions that increased the incidence of hypothermia were hypoproteinemia and cachexia (9).

Although the determinant influence of thyroid hormones on body temperature is well known, there are no specific reports on thyroid hormone plasma concentration and core temperature in elderly patients with acute illness. In the present study, mild rectal hypothermia was significantly associated with low T_3 and T_4 and high rT_3 plasma concentration and may reflect a previous, chronic hypometabolic state impairing the ability of these subjects to cope with an acute superimposed disease. It is suggested that malnutrition may be implicated in the pathogenesis of this chronic metabolic derangement.

Discriminant analysis showed that, in elderly patients with acute disease requiring an emergency hospital admission, the significant prognostic variables were rectal temperature,

TABLE 5
Thyroid status among hypothermic and normothermic patients

	Hypothermic (n = 11)	Normothermic (n = 53)
Thyroxine (nmol/L)	78 ± 17 (67–91)[1]	100 ± 25 (94–108)[2]
Triiodothyronine (nmol/L)	0.6 ± 0.3 (0.4–0.9)	1.1 ± 0.4 (0.9–1.2)[3]
Thyroid stimulating hormone (mU/L)	1.9 ± 1.4 (0.9–2.9)	1.4 ± 0.9 (1.1–1.6)
Reverse triiodothyronine (μmol/L)	18.5 ± 13.2 (9.2–26.2)	9.2 ± 5.3 (7.7–10.8)
APACHE II score[4]	20 ± 3 (18–23)	16 ± 3 (15–17)[5]
Death rate (%)	63	15[6]

[1] $\bar{x}$ ± SD; 95% CIs in parentheses.
[2,3,5,6] Significantly different from hypothermic patients: [2] $P = 0.009$, [3] $P = 0.003$, [5] $P = 0.0004$, [6] $P = 0.0022$.
[4] APACHE, Acute Physiologic and Chronic Health Evaluation.

TABLE 6
Clinical and nutritional status among patients with low and normal serum triiodothyronine concentrations

	Low triiodothyronine (n = 31)	Normal triiodothyronine (n = 36)
Rectal temperature (°C)	37.1 ± 1.1 (36.7–37.6)[1]	37.2 ± 0.5 (37.0–37.5)
Weight (kg)	55 ± 9 (55.0–51.5)	60 ± 13 (55.3–64.6)
Weight loss (%)	6.1 ± 7.7 (3.2–8.9)	5.6 ± 8.1 (2.8–8.4)
Prealbumin (mol/L)	33.5 ± 19.3 (26.5–40.5)	41.4 ± 20.7 (34.4–48.4)
Albumin (g/L)	32.0 ± 5.2 (30.1–33.9)	37.1 ± 6.2 (35.0–39.2)[2]
Thyroid stimulating hormone (mU/L)	1.2 ± 0.9 (0.8–1.5)	1.6 ± 1.1 (1.2–2.0)
Reverse triiodothyronine (μmol/L)	14.6 ± 9.1 (11.2–17.9)	6.5 ± 3.6 (5.2–7.7)[3]
APACHE II score[4]	18 ± 4 (16–20)	15 ± 2 (14–16)[3]
Death rate (%)	75	2525[5]

[1] $\bar{x}$ ± SD; 95% CIs in parentheses.
[2,3,5] Significantly different from patients with low triiodothyronine: [2] P = 0.0007, [3] P = 0.0001, [5] P = 0.008.
[4] APACHE, Acute Physiologic and Chronic Health Evaluation.

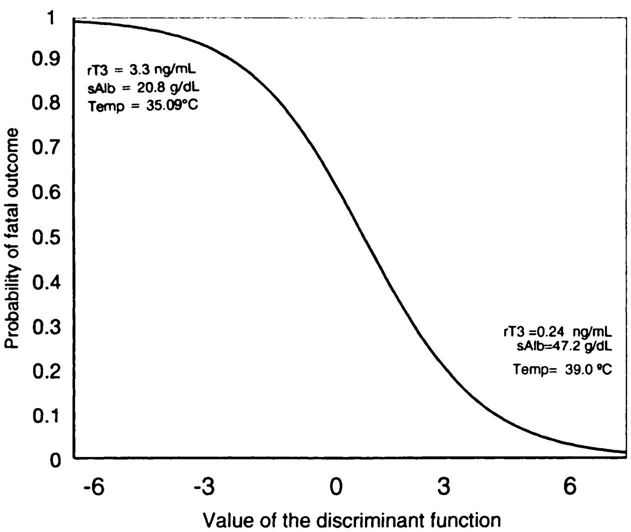

FIGURE 1. Relationship between the discriminant function and the probability of death. The two sets of values at each extreme of the sigmoid curve illustrate two examples of extremes values for each one of the variables used to obtain the discriminant function. rT_3, reverse triiodothyronine; sAlb, serum concentration of albumin; temp, rectal temperature. To convert sAlb to g/L, multiply by 10.0; to convert rT_3 to μmol/L, multiply by 15.4.

serum albumin concentration, and rT_3 concentration. Rectal temperature and serum albumin concentration can be easily checked at admission in most hospitals and, when abnormal, a 70% risk of death may be expected. Thus, it appears that this high-risk group of elderly patients may require a more specific metabolic support that may include closer monitoring, aggressive nutritional support, heating, and endocrine manipulation.

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