Yonsei Medical Journal
Vol. 44, No. 2, pp. 203 - 209, 2003

Nosocomial Infection of Malnourished Patients in an Intensive Care Unit

Songmi Lee[1,2], Misook Choi[1,2], Yongsook Kim[3], Jeongbok Lee[5], and Cheungsoo Shin[1,4]

[1]Nutrition Support Team; Departments of [2]Nutrition services, [3]Quality Improvement, and [4]Anesthesiology, Yongdong Severance Hospital, Yonsei University College of Medicine, Seoul, Korea;
[5]Department of Statistics, Korea University, Seoul, Korea.

Malnutrition is one of the most important factors for the development of nosocomial infection (NI). We performed a study of the correlation between abnormal nutritional factors and NI risk by investigating the patients who stayed longer than 3 days in the intensive care unit (ICU) of our university hospital. The patients were classified into three groups based on serum albumin levels and total lymphocyte counts (TLC). The criteria of Group I (well nourished group) were serum albumin level of 3.5 g/dl or higher and TLC of 1,400/mm^3 or higher. The criteria of Group III (severely malnourished group) were serum albumin of less than 2.8 g/dl and TLC of less than 1,000/mm^3. The other patients were classified as Group II (moderately malnourished group). The occurrences of NI were monitored during the study period and the APACHE III Score was calculated. The probability of first NI infection in Group III was 2.4 times higher than that in Groups I & II. The mortality rate of 20.5% was more significantly correlated with APACHE III Score than nutritional status. Nineteen (53%) of the total 36 NI patients were infected within 10 days after ICU admission and they all belonged to Group III. When we compared the gap period between infections, the time to first infection was significant.

Key Words: Malnutrition, nosocomial infection

INTRODUCTION

Nosocomial infection (NI), defined as a major contributor to hospital associated morbidity and mortality,[1] is any infection acquired in hospital that was not present or incubating prior to hospitalization.[2] The synergistic interaction of poor nutrition and superimposed infection increases the morbidity and mortality of hospitalized patients. Yet the importance of nutrition is still largely devaluated in hospital pratice.[3] In 1974, Blackburn reported the prevalence of hospital malnutrition.[4]

Now it is generally accepted that malnutrition is one of the most important risk factors for the development of NI. NI is a major contributor to hospital associated morbidity and mortality rates, especially in critically ill patients in the intensive care unit (ICU).[1] However, limited information was available about the correlation between malnutrition and NI in critically ill patients in ICU.

Thus, we designed the present study to investigate the incidence of malnutrition in a population of critical ill patients using simple diagnostic criteria and to determine whether malnutrition is correlated with poor outcome, defined as incidence of NI, longer hospital day and increased mortality.

MATERIALS AND METHODS

All patients admitted to general ICU of our university hospital in a recent 6 months period were included in this prospective study. Patients were excluded from the study if their ICU stay was shorter than 72 hours. Thereafter we also monitored the occurrence of NI for 3 months.

General information on age, sex and hospital stay was recorded for all the patients, and laboratory data on serum albumin, total lympho-

Received April 12, 2002
Accepted December 31, 2002

Reprint address: requests to Dr. Cheungsoo Shin, Department of Anesthesiology, Yongdong Severance Hospital, Yonsei University College of Medicine, 146-92 Dogok-dong, Kangnam-gu, Seoul 135-720, Korea. Tel: 82-2-3497-3522, 3520, Fax: 82-2-3463-0940, E-mail: cheung56@yumc.yonsei.ac.kr

cyte count (TLC), and hematocrit were collected at the time of admission. The APACHE (Acute Physiology, Age, Chronic Health Evaluation) III Score, known to predict hospital mortality risk for critically ill adult patients, was calculated.[5]

Serum albumin and TLC were selected for assessment of the degree of nutritional depletion. The patients were classified into one of three groups based on the levels of serum albumin and TLC. The criteria of Group I (well nourished group) were serum albumin level of 3.5 g/dl or higher and TLC of 1,400/mm^3 or higher. The criteria of Group III (severely malnourished group) were serum albumin of less than 2.8 g/dl and TLC of less than 1,000/mm^3. The others were classified as Group II (moderately malnourished group).

We used the NI data reported by the infection control surveillance system at our institution. The system included individual case study of patients reported to the infection control practitioner, as well as review of microbiological data and patients with positive cultures.

In this study, all the data were summarized by mean and standard deviation values for continuous variables and by frequency and percentage values for discrete variables. In order to understand the patients' infectious status, we counted the number of infections and compared the distribution of infection frequency among the three groups using Chi-squared test. The mean values of age, hospital stays and APACHE III score among the three groups were compared using Kruskal-Wallis test. We calculated Kaplan-Meier estimates of first infection time and survival time, and compared the distribution of these two variables among the three groups using log-rank test. As we observed recurrent infections in many patients, we applied the multivariate survival analysis proposed by Wei et al.[6] and Prentice[7] at al to compare differences in infection occurrence and gap period between the three groups. SAS V6.12 was used to analyze all the data.

RESULTS

One hundred and sixty one patients (102 male, 59 female) were selected. The patients with serum albumin level 3.5 g/dl or higher were 50 patients (31%), those with 2.8 g/dl or lower were 72 patients (45%). The patients with TLC 1,400 /mm^3 or higher were 93 patients (58%), those with 1,000/mm^3 or lower were 37 patients (23%) (Table 1).

Twenty-one patients (13%) satisfied the criteria for Group I (well nourished), 108 patients (67%) for Group II (moderately malnourished), and 32 patients (20%) for Group III (severely malnourished).

The most frequent diagnosis in the patients was sepsis, followed by cardiovascular disease, gastrointestinal failure and central nervous system disorder (Table 2).

To clarify the interaction between malnutrition status and NI, we investigated the difference of non-nutritional factors such as age, hospital stay and APACHE III score among the groups (Table 3).

There were a total of 50 cases of NI (36 patients) among the 161 patients (Table 4). The most common types of NI were urinary tract infection (40%), respiratory infection (22%) and bacteremia (14%).

The NI incidence rates were 19.1% (4 of 21 patients) for Group 1, 18.5% (20 of 108 patients) for Group II and 37.5% (12 of 32 patients) for Group III. The differences were, however, not

Table 1. Frequency Distribution of Serum Albumin Levels and TLC

Serum Albumin (g/dl)		TLC (/mm^3)	
Range	No. of patients (%)	Range	No. of patients (%)
≥ 3.5	50 (31)	≥ 1400	93 (58)
2.8 - 3.5	39 (24)	1000 - 1400	31 (19)
< 2.8	72 (45)	< 1000	37 (23)

TLC, Total lymphocyte counts.

statistically significant (Fig. 1, p=0.072). And Group III showed the highest NI multiple infection rate (Fig. 2).

We combined Group I and II, because the low NI incidence of Group I was not appropriate for log-rank test, and compared them with Group III. The probability of first NI infection in Group III was 2.4 times higher than in Groups I & II within 10 days of ICU admission, and showed significantly different distribution between two groups (p=0.029, Fig. 3).

On the other hand, the overall mortality rate was 20.5% for the three groups. And showed higher mortality rate of Group III than Groups I & II (p=0.001, Fig. 4).

Table 2. Main Diagnosis of the Study Population

Diagnosis	No(%)
Sepsis	26 (16.2)
Cardiovascular disease	22 (13.7)
Gastrointestinal failure	20 (12.4)
Central nervous system disorder	20 (12.4)
COPD, Respiratory failure	18 (11.2)
Cancer	15 (9.3)
Trauma	15 (9.3)
Electric surgery	10 (6.2)
Renal failure	10 (6.2)
Endocrine disorder	5 (3.1)
Total	161 (100.0)

COPD, Chronic obstructive pulmonary disease; No, Number of patients.

We also observed the association between nutritional status and total infection times using multivariate survival analysis (Table 5). The result showed that patients with severe malnutrition had a higher risk ratio in 1st and 2nd infection times (p=0.035 and p=0.075, respectively). And the overall probability of total infection was about 2.1 times higher in Group III than in Groups I & II (p=0.034). When we compared the gap periods between infections, the time to 1st infection was significant, but the period between 1st and 2nd infection was not significant. The overall risk ratio of gap periods tended to be significant (risk ratio=1.652, p=0.077).

DISCUSSION

Our data, whilst not new, were startling never-

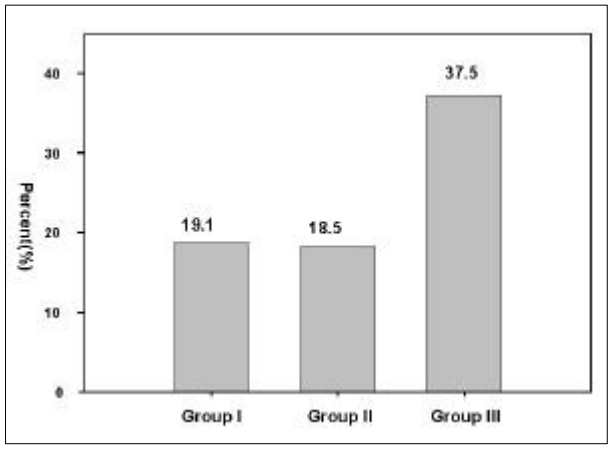

Fig. 1. Infection rates among groups.

Table 3. General Subject Characteristics

Variables	Group I (No=21)	Group II (No=108)	Group III (No=32)	p-value[1]
Hospital days	21 ± 16	26 ± 27	34 ± 31	0.302
Age (years)	59 ± 12	57 ± 16	61 ± 15	0.499
APACHE III[2]	41 ± 26	38 ± 19	47 ± 21	0.084

[1]Kruskal-Wallis Test.
[2]APACHE, Acute physiology age chronic health evaluation.
No, Number of patients.
Continuous data are given as mean ± standard deviation.

theless. We found that; a) malnutrition was still highly prevalent in critically ill patients; b) the presence of severe malnutrition had greater impact on NI; but c) malnutrition status on admission did not affect patient mortality.

Our result of 87% of the study population being malnourished appears to be higher than the 40% rate reported by Giner et al.[8] The infection incidence rate was 37.5% in Group III (severely malnourished group); also higher than the 10% reported by Giner et al. This is considered to be due to the difference in the study subjects. The subjects of this study were 161 patients out of 720 ICU patients, and the relatively healthy patients who were admitted to ICU for less than 72 hours were excluded from this study. Thus any comparison of incidence rate between this study and Giner's is considered inappropriate. The other possible reason is that no uniformly agreed definitions of malnutrition exist. Our malnutrition rate was higher than that reported in the literature,[8] but we consider that the malnutrition criteria in this study were within the generally accepted range for malnutrition criteria. There is no "golden standard" for determining nutritional status because there is no universally accepted clinical definition of malnutrition.

Patient's body weight is often not measured in critically ill patients. Especially, critically ill patients are often over hydrated to an extent that body weight may be increased by 6 to 12 kg.[9] So,

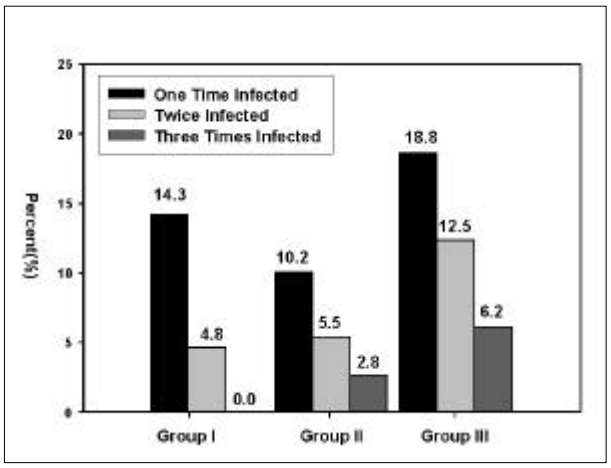

Fig. 2. Number of infection among the groups.

Table 4. Types of Nosocomial Infection

Nosocomial Infection	No. of patients (%)
Urinary tract	20 (40)
Respiratory	11 (22)
Bacteremia	7 (14)
Skin and soft tissue	6 (12)
Wound	2 (4)
Surgical wound	2 (4)
Nervous system	1 (2)
Gastrointestinal	1 (2)
Total	50 (100)

Table 5. Multivariate Survival Analysis of Infection Times

		Estimate ± SE	Risk Ratio	*p*-value
Multivariate Infection Times	1st Infection	0.748 ± 0.354	2.112	0.035*
	2nd Infection	0.920 ± 0.517	2.508	0.075
	3rd Infection	0.804 ± 0.916	2.234	0.38
	overall	0.752 ± 0.354	2.121	0.034*
Gap Times	- 1st Infection	0.748 ± 0.354	2.112	0.035*
	1st - 2nd Infection	0.201 ± 0.519	1.223	0.699
	2nd - 3rd Infection	0.087 ± 0.917	0.916	0.924
	overall	0.502 ± 0.284	1.652	0.077

*$p<0.05$.
SE, Standard error.

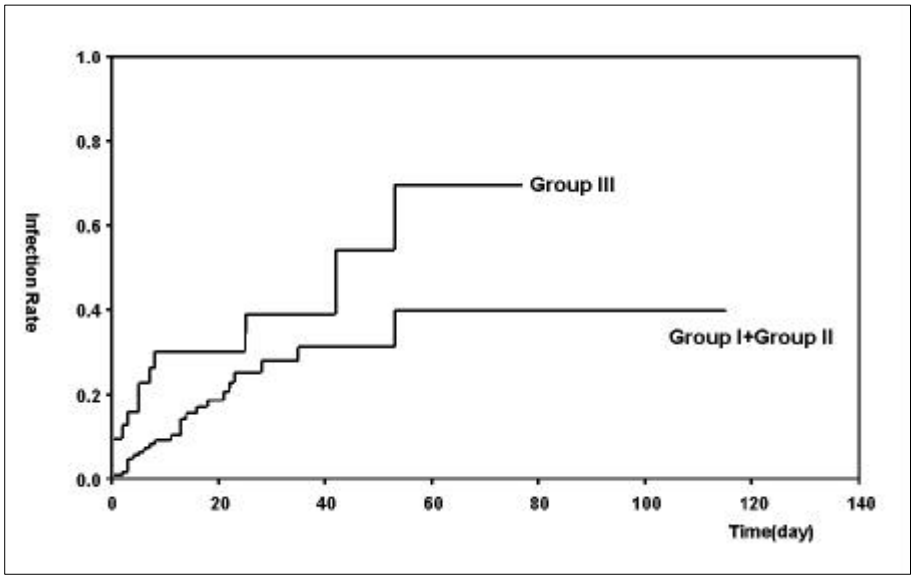

Fig. 3. Infection rate between Group I + Group II and Group III.

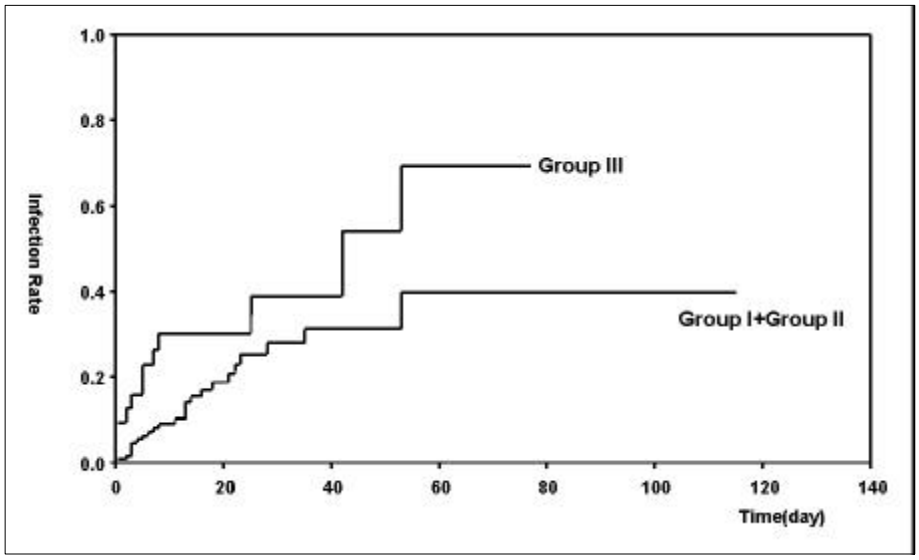

Fig. 4. Survival rate associated with the nutritional status.

body weight is not a reliable indicator of nutritional status in critical ill patients. Thus different anthropometric, biochemical, and immunologic parameters, as well as functional tests and indirect noninvasive techniques such as bioelectric impedance analysis, have been proposed to assess nutritional status. Other clinical surveys have investigated prognostic value by using a combination of biochemical, anthropometric, and immunological tests to increase the sensitivity and specificity of the diagnosis of malnutrition. Unfortunately, many of these indicators are not readily available. An ideal clinical marker of nutritional state should be widely available, easily reproducible, highly specific to nutritional state, and sensitive to its modifications. Unfortunately, no such marker is available.[10]

Simple and effective criteria for the identification of poor nutritional status are therefore warranted. It has been reported that serum albumin and TLC constitute an useful nutritional index to predict the risk of infection.[11]

Albumin is considered the first biochemical marker of malnutrition and has long been used in the assessment of hospital patients. Low levels of serum albumin reflect a dynamic balance of

hepatic production, distribution in the plasma space and protein loss from the vascular component. The greatest change in albumin level is due to redistribution between intravascular and extracellular components, as a result of which about 80% of the albumin pool becomes extravascular. Therefore a fall in albumin value is usually a better reflection of the metabolic response and its severity and duration than nutrition status per se.[12]

Even though serum albumin may not be a good indicator of nutritional status per se in critically ill patients, its predictive value in patient's out come has been recently emphasized.[13] It also has been suggested that a low serum albumin concentration correlates with an increased incidence of medical complications.[14]

Since lymphocytopenia reflects mainly decreased cell mediated immunity, one would expect only an increase in viral, fungal and intracellular bacterial infection, not in pyogenic infection.[15] However, few infections of this kind were identified in this study.

Two explanations may be advanced: First, in peripheral blood approximately 65% to 80% of the lymphocytes are T cells and approximately 8% to 15% are B cells.[14] Thus phenomena causing changes of T cell count are more likely to be associated with lymphocytopenia. Approximately two thirds of T cells are CD4 positive,[16] and these cells are usually affected by lymphocytopenia as the major cause. A risk of opportunistic infections occurs when the CD4 positive cell count falls below $0.2 - 0.3 \times 10^9/\ell$, which would correspond to TLC of approximately $0.4 \times 10^9/\ell$, depending on the degree to which CD8 positive T cells are affected.[17] This is a very low level of lymphocytopenia.

Second, since 25% of lymphocytes are B lymphocytes, TLC reflects humoral immunity in part, and therefore lymphocytopenia may indicate a deficiency in this system as well as cell mediated immunity.[18] More likely, lymphocytopenia reflects mainly a depressed cell mediated immunity, but this is only part a more widespread deficiency state which includes depressed humoral immunity and impaired phagocytosis. Moreover, the interaction between cellular and humoral immune systems is far greater than previously thought; a decisive factor in derangement of cellular immunity in malnutrition is the failure of formation of humoral agent and the transfer factor by the lymphocytes.[19]

Whereas the severe malnutrition group showed a higher incidence rate of infection, we couldn't find a difference between the groups in terms of mortality rate. We first thought that although infection was an important contributing factor in determining patient's prognosis, the more important factor is the degree of disease severity. As mentioned above, there was no significant difference in severity score between the groups in our study.

There were no major changes in primary outcomes (mortality and length of hospital stay). Length of stay may also vary with other factors and is usually a weak indicator of outcome. It is generally accepted that early mortality is related to the extent of the disease process, and that late mortality at 6 months may be influenced, at least in part, by nutrition.[20]

It has been suggested that malnourished patients with less severe degrees of illness appear to be most prone to suffer adverse consequences as a result of their malnutrition.[8] In other words, the negative effects of malnutrition on critically ill patients can not be clearly expressed because of the severity of illness.

The main outcome of this study was the result that severely malnourished patients in ICU were more likely to be infected, 2.1 times more in terms of total infection and 2.4 times more in terms of first infection, than moderately malnourished and well nourished patients.

REFERENCES

1. Singh-Naz N, Sprague BM, Patel KM, Pollack MM. Risk factors for nosocomial infection in critically ill children: A prospective cohort study. Crit Care Med 1996;24:875-8.
2. Schaffner W. Prevention and control of hospital- acquired infections. In: Bennett JC, Plum F, editors. Cecil Textbook of Medicine. 20th ed. Philadelphia: W.B. Saunders Co.; 1996. p.1548-53.
3. Scrimshaw NS. Malnutrition and nosocomial infection. Infect Control Hosp Epidemiol 1989:10:192-3.
4. Blackburn GL, Maine BS, Pierce EC Jr. Nutrition in the critically ill patient. Anesthesiology 1977;47:181-94.

5. Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognosis system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991;100: 1619-36.
6. Wei LJ, Lin DY, Weissfeld L. Regression analysis of multivariate incomplete failure time data by modeling marginal distributions. J Am Stat Assoc 1989;84:1065-73.
7. Prentice RL, Williams BJ, Peterson AV. On the regression analysis of multivariate failure time data. Biometrika 1981;68:373-9.
8. Giner M, Laviano A, Meguid MM, Gleason JR. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. Nutrition 1996;12:23-9.
9. Monk DN, Plank LD, Franch-Acras G, Finn PJ, Streat SJ, Hill GL. Sequential changes in the metabolic response in critically injured patients during the first 25 days after blunt trauma. Ann Surg 1996;223:395-405.
10. Manning EM, Shenkin A. Nutritional assessment in the critically ill. Crit Care Clin 1995;11:603-34.
11. Zagoren AJ, Burday M, Sonn RL, Cody R, Silverman D. Predicting postoperative complications by determinations of serum albumin, total lymphocyte count, and total neutrophil count. J Am Osteopath Assoc 1983; 82:768-73.
12. Klein S. The myth of serum albumin as a measure of nutritional status. Gastroenterology 1990;99:1845-6.
13. Spiekerman AM. Protein used in nutritional assessment. Clin Lab Med 1993;13:353-69.
14. Reinhardt GF, Myscofski JW, Wilkens DB, Dorbin PB, Mangan Jr. JE, Stannard RT. Incidence and mortality of hypoalbuminemic patients in hospitalized veterans. J Paren Ent Nutr 1980;4:357-9.
15. Good RA. Biology of the cell-mediated immune response - A review. In: Suskind RM, editor. Malnutrition and the immune response. New York: Raven Press; 1977. p.29-46.
16. Roitt IM. Essential immunology, 5th ed. London: Blackwell Scientific Publications; 1991. p.187-8.
17. Stewart GJ. The challenge: clinical diagnosis of HIV. Med J Aust 1993;158:31-4.
18. Lewis RT, Klein H. Risk factors in postoperative sepsis: Significance of preoperative lymphocytopenia. J Surg Res 1979;26:365-71.
19. Brown RE, Katz M. Passive transfer of delayed hypersensitivity reaction to tuberculin in children with protein calorie malnutrition. J Pediatr 1967;70:126-8.
20. Griffiths RD, Jones C, Palmer TEA. Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition. Nutrition 1997;13:295-302.