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Ueno, Kumiko
Department of Environmental Medicine and Infectious Disease, Graduate School of Medical Sciences, Kyushu University

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A Relationship between Febrile Illness, Serum Albumin Level and Mortality in Elderly Hospitalized Patients

Kumiko UENO

Department of Environmental Medicine and Infectious Disease (Director Professor : Jun Hayashi), Graduate School of Medical Sciences Kyushu University, Fukuoka 812-8582, Japan

Abstract The author sought to determine the etiology of febrile illness and risk factors influencing mortality in elderly patients. The patients, aged 65 years or older, were hospitalized in a geriatric hospital in Fukuoka City, Japan. A total of 405 febrile illness was diagnosed and the background, clinical features of the fever, and laboratory data were analyzed. Serum albumin levels were checked both at the onset and on the 8th day of fever in 140 patients. Of febrile illness of elderly patients, pneumonia is a principal disease with a high risk of mortality. Serum albumin level at the onset of fever and the reduction rate in the serum albumin level from baseline to day +8 after the onset of febrile illness were predictive factors of mortality within 30 days of fever. When examining febrile, elderly patients, checking the serum albumin level is useful for determining which patients are at high risk.

Key words: elderly patients, febrile illness, mortality, serum albumin level

Introduction

As the elderly population has increased in Japan, the number of the patients who are hospitalized for long periods of time has grown. Nosocomial febrile illness, defined as a fever occurring at least 48 hours after hospital admission[1], is a serious problem for elderly, hospitalized patients. The prevalence of nosocomial febrile illness has been estimated to be from 2% to 31% of all medical inpatients[1)6)7)14)]. Trivalle et al.[22] focused on elderly inpatients (>65 years of age) and found nosocomial febrile illness to be a common event. Once elderly patients with underlying disease or weakened immunity acquire an infection, their clinical condition often rapidly deteriorates with the addition of other diseases. To reduce the mortality rate by febrile illness, it is important to take measures to prevent nosocomial febrile illness in hospitalized, elderly patients and to clarify the related factors.

Several biochemical markers have been identified as having prognostic value for mortality and functional decline in community-dwelling, hospitalized, and institutionalized, elderly individuals[17]. Of these markers, serum albumin level has been the best studied, and has long been recognized an indicator, albeit crude, of the state of general health and nutrition of an individual[24]. This test is readily available and is included as part of many automated serum biochemistry batteries. Multivariate logistic analysis has revealed that several socioeconomic factors, including lifestyle[19], disease[3)19)], and age[3)20)], are associat-

ed with hypoalbuminemia.

Many investigators previously reported serum albumin level to be predictive of clinical outcome and mortality in elderly patients[5)9)]. However, they measured the serum albumin level only on admission. It is known that a lowering of the serum albumin level is a component of the acute phase response and can be expected when a patient has a fever, because the same cytokines that are pyrogenic also lower serum albumin. Whether or not the rate of the drop in the serum albumin level caused by an acute inflammatory reaction is of any predictive value has not been determined.

To determine the etiology of febrile illness and the risk factors influencing mortality in elderly hospitalized patients, the author diagnosed 405 patients with febrile illness and analyzed the underlying diseases, laboratory data, duration of fever, and the relation to mortality.

Materials and Methods

1. Patients

These data were collected between April 15, 1994 and April 14, 1995 at a 556-bed hospital in Fukuoka City, Japan, in which over 90% of the patients were 65 years or older. A febrile illness was defined as a fever above 37.5°C occurring after at least a 7-day period of temperature below 37.5°C. In total, 405 febrile illness from 405 patients (118 men, 287 women) (mean age 82.3 years : men 80.7, women 82.9) were analyzed. The physical examinations for all patients were conducted by the author to ensure uniformity in the collection of data. After all of the physical exam, laboratory analysis, and radiological exam data were collected, each case was examined and discussed by multiple doctors to agree on a final collective diagnosis.

The status of the underlying disease and general activities, including mental, physical, and nutritional condition, were also checked for each patient. Since many patients had multiple underlying diseases, it was sometimes difficult to determine the main one. In this study, each disease was counted separately. The underlying diseases of 405 patients included cerebrovascular disease in 181 patients (44.7%), cardiovascular disease in 176 (43.5%), chronic respiratory disease in 61 (15.1%), diabetes mellitus in 59 (14.6%), malignant tumor in 52 (12.8%), and others were 89 (22.0%). In addition, 3 other factors were measured : (1) activity of daily life : ambulant 148 (36.5%) and bedridden 257 (63.5%), (2) mental state : normal 130 (32.1%), borderline 168 (41.5%) and dementia 107 (26.4%), (3) nutritional state : normal 326 (80.5%), tube nutrition 17 (4.2%), and intravenous hyper nutrition 62 (15.3%). Of the 405 patients, 59 died within 30 days from the onset of fever and were assigned to a Non-survival group. The remaining 346 patients were assigned to a Survival group.

2. Blood sampling and laboratory examination

Samples were collected for blood tests and urinalysis. Bacterial cultures were done. All tests were performed before the start of therapy and on the 8th day. Chest X- rays were also done at the onset of febrile illness. White blood cell (WBC) count, C-reacting protein (CRP) volume, and serum albumin level were evaluated in this study.

Serum albumin levels were available for 140 (38 men and 102 women) of the 405 patients at two time points (onset of febrile illness and on the 8th day). The reduction rate of the serum albumin level between the

onset day and the 8th day were calculated and were shown as percentages. Normal standards of WBC count, CRP volume, and serum albumin level in this laboratory were as follows: WBC; 3900-9800 /μl (male), 3500-9100 /μl (female), CRP; 0.0-0.30 mg/dl, serum albumin level 4.0-5.0 g/dl.

3. Diagnosis criteria

Pneumonia: Cough, sputum, moist rale, and the presence of radiographycally typical infiltration during the clinical course. Influenza: Over 4 fold elevation of hemagglutinin inhibition titer in addition to typical symptoms of myalgia, arthralgia and high fever. Urinary tract infection (UTI): High white blood cell and bacteria counts (numerous counts / hpf) in urine sediment and urine culture, collected using a catheter, with bacteria above 10^4 CFU / ml on the onset day. All these positive findings had to diminish by the 8th day.

4. Statistical analyses

To compare the WBC count, CRP volume, and serum albumin level of the onset day with the duration of fever between the Survival-group and Non-survival group, the t-test was used. Chi-square test, ANOVA analysis, and Mann-Whitney's U-test were used among the groups divided by factors such as underlying disease, activity of daily life, mental state, nutritional state, and characteristics of fever. Spearman's correlation analysis was used to examine the correlation between the serum albumin reduction rate and other variables such as duration of fever, serum albumin level at onset, WBC count, CRP volume at onset, and age. To determine the factors affecting mortality, logistic regression analysis was used for various factors at onset such as duration of fever, serum albumin level, WBC count, CRP volume, etiology of febrile illness, age, and underlying diseases.

Results

Comparison of background characteristics found significantly more men in the Non-survival group (42.4%) than in the Survival-group (26.9%) ($p=.023$) and the rate of malignant tumor to be significantly higher in the Non-survival group patients 22 (37.2%) of 59 than in the Survival group patients 30 (8.7%) of 346 ($p<.001$). Ambulant patients were significantly fewer in the Non-survival group (13.6%) than in the Survival group (40.5%) ($p<.001$). The rate of intravenous hyper nutrition was significantly higher in the Non-survival group (47.5%) than in the Survival group (9.8%) ($p<.001$) (Table 1).

Table 2 shows the etiology of febrile illness in 405 hospitalized elderly patients grouped by Non-survival and Survival. The etiology of febrile illness included 160 patients (39.5%) who had respiratory tract infection, 82 (20.2%) with UTI, 33 (8.1%) with bacteremia, 29 (7.2%) with other infections, 9 (2.2%) with malignant tumor, 2 (0.5%) with autoimmune disease, 1 (0.2%) with other disease, and the remaining 89 (22.0%) with unknown cause. Of 160 patients with respiratory tract infection, 46 (28.8%) had influenza, 44 (27.5%) pneumonia, 40 (25%) upper respiratory tract infection, 28 (17.5%) bronchitis, and the remaining 2 (1.3%) pleuritis. Infection was found in 304 (75.1%) of the patients with febrile illness. The etiology of febrile illness between 59 Non-survival group patients and 346 Survival group patients was compared. The rate of pneumonia was significantly higher in the Non-survival group 14 (23.7%) than in the Survival group 30 (8.7%) ($p<.001$).

A comparison of WBC count, CRP vol-

Table 1 A comparison of characteristics of background between the Survival group and the Non-survival group in 405 patients

Background factors		Survival group (n=346 patients) No. of patients (%)	Non-survival group (n=59 patients) No. of patients (%)	p-value
Gender	Men	93 (26.9)	25 (42.4)	.023
Underlying disease				
Cerebrovascular disease		153 (44.5)	28 (47.5)	.644
Cardiovascular disease		149 (43.1)	27 (45.8)	.699
Chronic respiratory disease		45 (13.0)	16 (27.1)	.005
Diabetes mellitus		48 (13.9)	11 (18.6)	.337
Malignant tumor		30 (8.7)	22 (37.2)	<.001
Other disease		72 (2.1)	17 (28.9)	.170
Activity of daily life	Ambulant	140 (40.5)	8 (13.6)	
	Bedridden	206 (59.5)	51 (86.4)	<.001
Mental state	Normal	119 (34.4)	11 (18.6)	
	Borderline	138 (39.9)	30 (50.8)	
	Dementia	89 (25.7)	18 (30.5)	.055
Nutritional state	Normal	296 (85.5)	30 (50.8)	
	Tube nutrition	16 (2.9)	1 (1.7)	
	Intravenous hyper nutrition	34 (9.8)	28 (47.5)	<.001

ume, serum albumin level, and duration of febrile illness was conducted between the Survival and the Non-survival groups. WBC counts and CRP volume were signifi-

Table 2 A comparison of etiology of nosocomial febrile illnesses between Survival group and Non-survival group in 405 patients

Etiology	Survival group No. of patients	%	Non-Survival group No. of patients	%	Total No. of patients	%
1. Respiratory tract infection	143	41.3	17	28.8	160	39.5
Pneumonia	30	8.7*	14	23.7†	44	
Bronchitis	26		2		28	
Upper respiratory tract infection	40		0		40	
Influenza	46		0		46	
Pleuritis	1		1		2	
2. Urinary tract infection	77	22.3	5	8.5	82	20.2
3. Bacteremia	24	6.9	9	15.3	33	8.1
4. Other infection	25	7.2	4	6.8	29	7.2
Decubitus	8		1		9	
Enterocolitis	8		1		9	
Cholangitis, cholecystitis	6		1		7	
Phlegmon	2		1		3	
Herpes zoster	1		0		1	
5. Malignant tumor	2	0.6	7	11.9	9	2.2
6. Autoimmune disease	1	0.3	1	1.7	2	0.5
7. Other diseases	0	0	1	1.7	1	0.2
8. Unknown origin	74	21.4	15	25.4	89	22.0
Total	346	100.0	59	100.0	405	100.0

(*Vs† ; p<.001)

cantly higher in the Non-survival group patients (WBC; 11,959 ± 7,940 /μl, CRP; 7.65 ± 5.30 mg /dl) than in the Survival group patients (WBC; 8,128 ± 4,299 /μl, CRP; 4.79 ± 4.43 mg /dl) ($p<.001$ respectively). The serum albumin level was significantly higher in the Survival group (3.46 ± 0.52 g /dl) than in the Non-survival group (2.77 ± 0.56 g /dl) ($p<.001$). Duration of febrile illness was significantly longer in the Non-survival group (3.8 ± 2.3 days) than in the Survival group (2.3 ± 1.5 days) ($p<.001$) (Table 3).

To search for predictive factors that would influence the mortality of elderly patients within 30 days of a febrile illness, multiple logistic regression analysis was done for various factors such as duration of fever, serum albumin level, WBC count, CRP volume, etiology of febrile illness, age and underlying diseases. The serum albumin level at onset, underlying disease with malignant tumor, WBC count, and duration of febrile illness were significantly associated with mortality ($p<.001$, respectively) (Table 4).

Of 405 elderly patients, 140 (Survival group; 117 and Non-survival group; 23) had serum albumin levels measured at onset and on the 8th day of febrile illness. The mean reduction rate of the serum albumin level from onset to the 8th day in these 140 patients was 6.3 %. Table 5 shows a comparison of the serum albumin level and the reduction rate between the Survival group and the Non-survival group. The reduction rate of the Non-survival group was significantly higher (13.2%) than that of the Survival group (5.0%) ($p=.025$).

Table 6 shows a comparison of the serum albumin level and the reduction rate among the groups divided by the duration of fever. The patients were divided into a 1 day group (51 patients; Survival 46, Non-survival 5) and an over 2 days group (89 patients; Survival 71, Non-survival 18). The reduction rate of the Non-survival group was significantly higher than that of the Survival group in both the 1 day group (Survival group; 1.6% and Non-survival group; 8.0%) and over 2 days group (Survival group; 7.2% and Non-survival group; 14.6%) ($p=.094$, $p=.0014$, respectively). The causes of fever in 5 Non-survival patients (one-day fever) were UTI, bacteremia, enterocolitis, and two of undefined origin. They died on 17, 11, 15, 17, and 24 days after fever, respectively.

To clarify contributing factors to the reduction of the serum albumin level, gender, background, underlying disease, grade of fever, etiology of febrile illness, and other variables such as age, duration of fever, WBC count, CRP volume, and serum albumin level at onset were compared (Table 7). The reduction rate was significantly higher in patients fed by intravenous hyper nutrition than in those fed by normal and tube

Table 3 A comparison of white blood cell (WBC) count, C-reacting protein (CRP) volume, serum albumin level, and duration of nosocomial febrile illness (NFI) between Survival and Non-survival group

Laboratorydata		Survivalgroup (346 patients)	Non-Survivalgroup (59 patients)	p-value (t-test)
WBC count	mean±SD (/μl)	8,128±4,299	11,959±7,940	<.001
CRP volume	mean±SD (mg/dl)	4.79±4.43	7.65±5.30	<.001
Albumin level	mean±SD (g/dl)	3.46±0.52	2.77±0.56	<.001
Duration of NFI	mean±SD (days)	2.3 ±1.5	3.8 ±2.3	<.001

Table 4 Factors affecting mortality within 30 days of febrile illness among 405 patients

Variable	Odds ratio	95 % Confidence interval		p-value
		lower	upper	
Albumin level at onset	0.11	0.05	0.23	0.0000
Underlying disease with malignant tumor	5.79	2.47	13.60	0.0001
White blood cell count	3.14	1.72	5.75	0.0001
Duration of febrile illness	1.69	1.26	2.26	0.0004

nutrition (p=.003). Patients with fever > 38.0 °C at onset had a significantly higher reduction rate of serum albumin level than those with 37.5 °C-38.0 °C fevers (p=.048). The reduction rate of serum albumin in patients with bacteremia (13.1 %) and with influenza (10.4 %) was significantly higher than in those with UTI (3.3 %) (p=.001, p=.003, respectively). The reduction rate was significantly correlated with duration of fever >38.0 °C (p<.001). However, it was not correlated with age, duration of fever 37.5-38.0 °C, WBC count, CRP volume, or serum albumin level at onset. Among all these variables, duration of fever >38.0 °C was the independent factor most directly related to the reduction rate of the serum albumin level (stepwise linear regression analysis; p<.001).

To determine the risk factors and to identify possible correlations between these risk factors, a logistic regression analysis was used for various factors such as duration of fever, serum albumin level at onset, WBC count, CRP volume, etiology of febrile illness, age, and underlying diseases. The serum albumin level at onset and the reduction rate of albumin level were significantly correlated with mortality (p=.0000, p=.0008, respectively) (Table 8).

Discussion

The finding that 75.1% of the institutionalized elderly patients (mean patient age, 82.3 years) with febrile illness had infectious diseases is similar to that of Trivalle et al.[22] (74.2%) (patients age, >65 years). In other studies, the frequency of infectious nosocomial febrile illness was 56% (mean patient age, 59 years) by Arbo et al.[1] and 67% (mean patient age, 66 years) by Filice et al.[6]. When the age of our patients is considered, the difference in these results seems to indicate that the frequency of infectious, nosocomial febrile illness increases with age. This finding supports previous studies that have shown that elderly patients are at a particularly high risk of developing nosocomial infection[8)21)].

Pneumonia continues to be a principal

Table 5 A comparison of serum albumin level and reduction rates between the Survival group and Non-survival group in 140 Patients

Gender	Survival group				Non-survivalgroup				Total			
	No. of patients	Albumin level mean±SD(g/dl) at onset	Albumin level mean±SD(g/dl) 8th day	Reduction rate mean±SD (%)	No. of patients	Albumin level mean±SD(g/dl) at onset	Albumin level mean±SD(g/dl) 8th day	Reduction rate mean±SD (%)	No. of patients	Albumin level mean±SD(g/dl) at onset	Albumin level mean±SD(g/dl) 8th day	Reduction rate mean±SD (%)
Men	28	3.28±0.56	3.19±0.47	1.7±12.1	10	2.56±0.33	2.43±0.36	3.8±16.0	38	3.09±0.60	2.99±0.55	2.2±13.1‡
Women	89	3.47±0.49	3.26±0.51	6.0± 8.4	13	3.07±0.54	2.52±0.55	20.4±12.0	102	3.42±0.51	3.17±0.57	7.9±10.1§
Total	117	3.42±0.53	3.24±0.50	5.0± 9.5*	23	2.88±0.47	2.48±0.46	13.2±15.7†	140	3.33±0.55	3.12±0.57	6.3±11.2

(*Vs†; p=.025, ‡Vs§; p=.028)

Table 6 A comparison of serum albumin level at onset, 8th days after fever, and reduction rate of two groups divided by the duration of fever in the Survival group and Non-survival group in 140 patients

Duration of fever (days)	Survival group				Non-survivalgroup			
	No. of patients	Albumin level mean±SD (g/dl) at onset	Albumin level mean±SD (g/dl) 8th day	Reduction rate mean±SD (%)	No. of patients	Albumin level mean±SD (g/dl) at onset	Albumin level mean±SD (g/dl) 8th day	Reduction rate mean±SD (%)
1	46	3.47±0.48	3.40±0.28	1.6 ±8.1*	5	2.72±0.57	2.45±0.42	8.0± 6.0†
over 2	71	3.40±0.53	3.15±0.37	7.16±9.8‡	18	2.88±0.52	2.48±0.34	14.6±16.0§

(*Vs†; p=0.094, ‡Vs§; p=0.014)

cause of death world-wide. According to official statistics in the United States, pneumonia and influenza infections are the fifth leading causes of death in persons aged 65 years or older[13]. Koivula et al.[12] also reported that one third of the elderly population were at increased risk of contracting pneumonia. The present study confirmed pneumonia to be an important febrile disease related to non-survival among elderly patients. These population-based data suggest the necessity of effective pneumonia prevention programs.

Serum albumin level is a critical marker of mortality in healthy, elderly persons[4][11][18]. The level on admission is also a valuable predictive marker of mortality, length of stay, and readmission in elderly patients[5][9]. Therefore, physicians carefully monitor serum albumin levels by age[3][20] and other life style factors[19], and make an effort to elevate the serum level. Reuben et al.[16] suggested the potential benefit of a nurse- administered assessment coupled with protocols to address remediable contributors to hypoalbuminemia. We previously reported that the incidence of febrile illness increased with decline of serum albumin levels[10]. Moreover, a reduction in the serum albumin level was reported in the acute phase of inflammatory response[2][15].

This study demonstrated that the serum albumin level at onset of febrile illness was associated with the prognosis of hospitalized, elderly patients. The serum albumin level was significantly reduced at the 8th day of febrile illness, and the reduction rate was related to duration of fever over 38.0 °C. The reduction rate of the Non-survival group was significantly higher than that of the Survival group.

Restrictions of this study included that the reduction rate could only be measured in patients who survived till the 8th day and the lack of data to show the degree of reduction in patients who died within 7 days after fever. Furthermore, the standard manual for use of anti-pyretics could not be defined exactly because the general conditions of our febrile patients were quite different and the drugs used depended on the clinical conditions.

Because the Non-survival group was defined as patients who died within 30 days after fever, the diseases causing the fever were not always the most important in final diagnosis of death. In these cases, there was the possibility that the death did not occur because of the disease causing febrile illness, but from the degradation of nutritional or/and immunological condition. Febrile illness may cause a detorioration of the general health condition of aged patients.

Table 7 A comparison of characteristics of background and characteristics of fever among 140 patients to contribute the reduction of serum albumin level from the 1st day to the 8th day

	Variable	No. of patients	Reduction rate mean±SD(%)	Correlation coefficient (r-value)	p-value	Statistical method
Gender:	Men	38	2.2±13.1			
	Women	102	7.8±10.1		.028	Mann-Whiteny's U-test
Nutritional state:	Normal	110	5.0±10.1			
	Tube nutrition	7	4.1± 8.2			
	Intravenous hyper nutrition	23	13.5±14.2		.003	ANOVA
Grade of fever:	>38.0°C	83	7.7±12.0			
	37.5°C<BT≦38.0°C	57	4.3± 9.6		.048	Mann-Whiteny's U-test
Etiology of NFI:	Bacteremia	10	13.1±12.8*			
	Influenza	16	10.4±11.0‡			
	Pneumonia	11	6.6± 8.0			
	Upper respiratory tract infection	13	6.2± 8.5			
	Urinary tract infection	35	3.3± 7.0†§			
	Other disease	19	4.7± 6.8			
	Unknown origin	35	6.3±11.2		.004	ANOVA
Duration of febrile illness (>38.0°C)		140		0.366	.0001	Spearman's rank correlation
Maximal body temperature		140		0.168	.047	Spearman's rank correlation
Albumin level atonset		140		0.155	.068	Spearman's rank correlation
CRP		140		0.101	.239	Spearman's rank correlation

(*Vs†; p=.001, ‡Vs§; p=.003)

The fact of that the reduction rate of one day fever of the Non-survival group is significantly higher than that of the Survival group suggests that the influence of the fever in the Non-survival group was larger than that of the Survival group. When elderly patients acquire a serious febrile disease with high fever (>38.0 °C), a rapid fall of serum albumin is seen, probably due to the fact that elderly patients have less functional reserve capacity. This parameter may be a clue to the mechanisms acting on febrile, elderly patients. Further physiological study is needed to explain this mechanism.

In our previous study, the number of one day fevers was nearly half[23]. On the other hand the symptoms of elderly patients are not typical as those of the younger patients. Sometimes a serious disease that leads to death is masked by these febrile illnesses. Clinical physicians must pay especially careful attention to elderly patients. This study suggests that the reduction rate of the serum albumin level is a useful indicator for identifying febrile, elderly patients who are at high risk.

On the other hand, a lowering of the

Table 8 Factors affecting mortality within 30 days of febrile illness among 140 patients

Variable	Odds ratio	95% Confidence interval lower	upper	p-value
Albumin level at onset	0.056	0.014	0.229	0.0000
Reduction rate of albumin level	0.919	0.868	0.973	0.0008
Maximal body temperature	0.264	0.066	1.065	0.0486
Duration of febrile illness	1.680	0.976	2.891	0.0531

serum albumin level doesn't always cause death directly, but it seems to play a role in the illness. This has been shown in patients with influenza, which is often fatal for the elderly. The serum albumin reduction rate for influenza was as high as that of bacteremia, but no patients died from influenza in this survey. In the case of influenza, other factors e.g. bacteria-related, can play a role in the processes leading to the death of the patients.

In any case, a low level of serum albumin often induce high frequency of febrile illness and can result in a critical condition. Adding a low level of serum albumin to some other factor can lead to a critical situation for the patients.

When a low albumin level is induced by aging or poor nutrition, some patients have weakened aspiration. Patients with difficulty aspirating often progress to aspiration pneumonia, and the level of serum albumin decreases. In this survey, patients who had difficulty eating used nasal tube nutrition or IVH. Nasal tube nutrition and IVH may have caused recurrent fever. It seems possible that mortality and the frequency of fever decrease with improvement of nutritional state. Percutaneous endscopic gastrostomy is induced in this hospital to support the nutritional state and to prevent aspiration pneumonia. The frequency of febrile illness and mortality after febrile illness related to this procedure must be investigated to clarify the effectiveness.

In conclusion, pneumonia is a principal disease in elderly patients with febrile illness. The serum albumin level at the onset of fever and the serum albumin reduction rate from the onset to the 8^{th} day have predictive value for the prognosis of elderly, hospitalized patients.

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高齢者入院患者における発熱疾患と血清アルブミン値及び死亡との関連性

九州大学大学院医学研究院感染環境医学分野（指導：林　純　教授）
上　野　久美子

高齢者入院患者の発熱疾患の原因と死亡に影響する危険因子を調べることを目的として405例の発熱疾患について原因，背景因子，臨床的発熱の特徴，検査データー，アルブミン値などを解析した．このうち，140例については発熱初日と8日目の2時点での血清アルブミン値をチェックした．発熱の原因では，肺炎が死亡との関連が高く重要な疾患であった．血清アルブミン値の低値は発熱後30日以内の死亡の予測因子であった．発熱の影響で8日目の血清アルブミン値は減少し，減少率も死亡との関連性が高かった．発熱後アルブミン値をチェックすることは，死亡の可能性の高いグループを把握する手段として日常の臨床で役に立つことが示唆された．