Treatment outcome of elderly patients with aggressive adult T-cell leukemia-lymphoma: Nagasaki University Hospital experience

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Running title: Outcome of elderly patients with aggressive ATL

Original article

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Abstract

VCAP (vincristine, cyclophosphamide, doxorubicin, and prednisone)-AMP (doxorubicin, ranimustine, and prednisone)-VECP (vindesine, etoposide, carboplatin, and prednisone) is a standard regimen for aggressive adult T-cell leukemia-lymphoma (ATL). However, the efficacy of this regimen has not been fully elucidated for patients aged 70 years or older. Here, we retrospectively analyzed elderly patients with aggressive ATL at Nagasaki University Hospital between 1994 and 2010 to assess treatment outcomes. Of 148 evaluable patients, 54 were aged 70 years or older at diagnosis. The median survival time (MST) and overall survival (OS) at two years in elderly patients were 10.6 months and 22.1%, respectively. Thirty-four patients received VCAP-AMP-VECP as the initial treatment, although the doses were reduced for most patients. In these patients, MST and OS at two years were 13.4 months and 26.6%, respectively. Eleven of 34 patients (32%) received maintenance oral chemotherapy after two or three cycles of VCAP-AMP-VECP, and MST and OS at two years were 16.7 months and 32.7%, respectively. Our results suggest that the VCAP-AMP-VECP regimen may be effective and that maintenance oral chemotherapy may be considered as a therapeutic option for elderly patients with aggressive ATL.

Keywords: adult T-cell leukemia-lymphoma (ATL), elderly patients, chemotherapy

Introduction

Adult T-cell leukemia-lymphoma (ATL) is a distinct peripheral T-cell malignancy associated with human T-lymphotropic virus type I (HTLV-1) [1-4]. Aggressive ATL (i.e., acute, lymphoma, or unfavorable chronic type) generally has a poor prognosis and has been considered a target of chemotherapy [5-7]. However, a poor treatment outcome has been reported with chemotherapy for aggressive ATL. The VCAP (vincristine, cyclophosphamide, doxorubicin, and prednisone)-AMP (doxorubicin, ranimustine, and prednisone)-VECP (vindesine, etoposide, carboplatin, and prednisone) regimen was developed as an intensified regimen, and efficacy has been reported for aggressive ATL [8, 9]. In the regimen, the interval between courses of chemotherapy was shortened to increase the dose intensity with administration of granulocyte-colony stimulating factor, and ranimustine and carboplatin were incorporated because the activity of these agents is not affected by the expression of P-glycoprotein, a possible mechanism of therapy resistance in ATL. The longer overall survival (OS) at 3 years and higher complete remission (CR) rate with VCAP-AMP-VECP compared with CHOP (cyclophosphamide, doxorubicine, vincristine, and prednisone)-14 have been reported for previously untreated aggressive ATL in a prospective randomized study [9]. The median survival time (MST) was reported to be 13 months, and the OS at 3 years was 24% for patients treated with VACP-AMP-VECP. Thus, this regimen is considered a standard treatment for patients with aggressive ATL. However, patients older than 70 years were not included in the clinical trial. Thus, the efficacy of this regimen in elderly ATL patients has not been elucidated.

In Western countries, the efficacy of anti-viral therapy (combination of the antiretroviral agents, interferon alpha and zidovudine) has been reported and adopted for the treatment of ATL [10]. However, the outcome of this treatment was not sufficient for aggressive ATL. The outcome of anti-viral therapy for lymphoma-type ATL was reported to be inferior to that of chemotherapy. Furthermore, the reported result of anti-viral therapy for acute-type ATL was not superior to the outcome of VCAP-AMP-VECP [9,10]. In addition, these drugs are not approved for the treatment of ATL in Japan.

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has been adopted for the treatment of aggressive ATL, and its efficacy has been reported [11-13]. However, the high therapy-related mortality remains a problem, and generally allo-HSCT cannot be used in patients older than 70 years. Thus, the optimal treatment of elderly patients has not been established.

A nationwide survey of ATL was carried out in Japan between 2006 and 2007 [14]. According to this survey, the age of ATL patients shifted toward older ages compared to previous nationwide studies, and the mean age gradually increased from 52.7 years in the first survey (cases before 1980) to 61.1 years in the ninth survey (1996-1997), and finally to 66.0 years in the current survey (median: 67 years, range: 19-94 years). Therefore, establishment of the optimal treatment strategy for elderly ATL patients is an important issue. However, the treatment outcome of elderly patients with aggressive ATL has not been evaluated.

In this study, we retrospectively investigated the outcome of patients 70 years or older with aggressive ATL in our hospital. The purpose of this study was to evaluate the treatment outcome in

clinical practice and to provide baseline data for treatment of elderly ATL patients.

Patients and methods

Patients

We evaluated a total of 196 previously untreated patients with aggressive ATL (i.e., acute, lymphoma, or unfavorable chronic type) who were admitted to the Nagasaki University Hospital between January 1994 and December 2010. Clinical subtypes of ATL were classified based on Shimoyama criteria [5]. The unfavorable chronic type of ATL was defined by the presence of at least one of the following three factors: low serum albumin (Alb), high serum lactate dehydrogenase (LDH), or high blood urea nitrogen (BUN) concentration [6]. Diagnosis of ATL was made based on clinical features, the presence of anti-HTLV-1 antibody, histologically and/or cytologically proven mature T-cell malignancy, and monoclonal integration of HTLV-1 proviral DNA into tumor cells in the evaluable cases. Of the 196 patients, 48 patients were excluded: 13 patients were excluded due to missing data at diagnosis, and 35 patients who had undergone allo-HSCT were also excluded (Figure 1). We conducted the study with the remaining 148 eligible patients. Of these patients, 54 patients were 70 years or older (elderly group). The remaining 94 patients who were under 70 years old were designated as the younger group. Data were collected and updated by October 2012.

Clinical Data

We collected information regarding age, sex, clinical subtype, white blood cell (WBC) count, neutrophil

count, total lymphocyte count, platelet count, serum total protein, serum Alb, LDH, BUN, soluble interleukin-2 receptor (sIL-2R), serum corrected calcium; serum calcium + (4 − Alb), Ann Arbor stage, performance status (PS) according to the Eastern Cooperative Oncology Group (ECOG), B symptoms (i.e., fever of unknown origin, loss of weight, or nocturnal sweating), and initial treatment. We defined leukemic stage IV disease as the presence of more than 1% abnormal lymphocytes in peripheral blood [15]. This retrospective, nonrandomized, observational study that used existing data was granted exemption from the institutional review board, and the requirement for written informed consent was waived.

Treatment and response

Basically, patients with aggressive ATL were treated with the VCAP-AMP-VECP regimen if their general condition was adequate. Patients who were not candidates for the full dose treatment received a dose-reduced VCAP-AMP-VECP regimen, which became the second treatment option. Patients with a worse condition were treated with other, less toxic regimens. Our study had no strict criteria for the selection of the treatment regimen or for the degree of the dose reduction. The final decision of the choice of the treatment regimen was made by each attending physician. Patients who received at least one cycle of the full dose or dose-adjusted VCAP-AMP-VECP as the initial treatment were assigned to the VCAP-AMP-VECP group, because it was difficult to distinguish the patient treated with VCAP regimen from those treated with dose-reduced CHOP-like regimen for the initial treatment in the retrospective analysis. The remaining patients were assigned to the other treatment group. In the elderly group, no patient was treated

with mogamulizumab, an anti-CC chemokine receptor 4 monoclonal antibody, at the point of final analysis of this study. In some elderly patients treated with the VCAP-AMP-VECP regimen, the treatment was stopped after two or three cycles of the regimen, and maintenance oral chemotherapy was administered that was mainly composed of etoposide and/or sobuzoxane and/or prednisone. The response criteria were divided into four categories: CR, partial remission (PR), stable disease (SD), and progressive disease (PD). Responses were defined as follows: CR, disappearance of all disease; PR, ≥50% reduction of measurable disease; SD, failure to attain CR or PR, but not PD; PD, new or increased lesions according to the Response Criteria for ATL [16]. In this study, the best response was assessed regardless of the duration of the response.

Statistical analysis

Comparison among groups was performed with the χ^2 statistic or Fisher's exact test as appropriate for categorical variables, and the Mann-Whitney U test for continuous variables. OS was calculated from the time of diagnosis to the date of death from any cause or to the last follow-up date. Survival curves were estimated using the Kaplan-Meier method and compared using the log-rank test. The 95% confidence interval (CI) of OS at 2 years was calculated. All tests were two-sided, and $P < 0.05$ was considered significant in all analyses. All statistical analyses were performed with Prism 6.0 software (GraphPad Software, San Diego, CA).

Results

Patient characteristics

We conducted the study with the 148 eligible patients (Figure 1). The clinical characteristics of all patients by age are summarized in Table 1. Ninety-four patients were in the younger group, and 54 patients were in the elderly group. WBC count, neutrophil count, and total lymphocyte count were significantly increased in the younger patients compared with those in the elderly group. The initial treatment was also different in the two groups. In the elderly group, the doses of VCAP-AMP-VECP were reduced in most patients. We found no difference in other clinical parameters between the groups. The median follow-up time for the survivors was 12.9 months (range: 0.2-201.5 months). Ninety-seven of 148 patients (65.5%) received VCAP-AMP-VECP as the initial treatment, 45 patients (30.4%) received other treatments, and six patients (4.1%) received only supportive care.

Survival of the patients

In the younger group, MST and OS at 2 years were 11.7 months and 26.4% (95% CI: 17.2-36.6%), respectively, whereas in the elderly group, MST and OS at 2 years were 10.6 months and 22.1% (95% CI: 11.6-34.8%), respectively (Figure 2). Although MST and OS at 2 years in the younger group tended to be better than those in the elderly group, no significant difference was observed between the two groups (P = 0.28; log-rank test).

Survival and response of the elderly patients

The clinical characteristics of the elderly patients by initial treatment are summarized in Table 2. The median follow-up time for the survivors was 22.2 months (range: 0.2-121.1 months). Thirty-four out of

54 patients (63.0%) received the VCAP-AMP-VECP regimen as the initial treatment, whereas 16 patients (30.0%) received other treatments. Four patients received only supportive care. We observed a statistically significant difference in age, WBC count, and total lymphocyte count between the VCAP-AMP-VECP group and the other treatment group (data not shown). The doses were reduced from the start of the chemotherapy in 31 out of 34 patients (91.2%) treated with the VCAP-AMP-VECP regimen. Of the 16 patients who received other treatments, 7 patients had CHOP/CHOP-like treatment, 3 patients had single agent treatment, 4 patients had other combination therapy, and 2 patients had radiation therapy. In the VCAP-AMP-VECP group, MST and OS at 2 years were 13.4 months and 26.6% (95% CI: 12.6-43.0%), respectively, whereas in the other treatment group, MST and OS at 2 years were 5.4 months and 15.5% (95% CI: 2.6-38.7%), respectively (Figure 3). In elderly patients treated with the VCAP-AMP-VECP regimen as the initial treatment, the survival curve was similar to the reported result in a clinical study of patients older than 56 years and younger than 70 years [9]. The overall response rate (CR+PR) was 75% (24/32; two patients were unknown) after two or three cycles of VCAP-AMP-VECP, and the rate of completion of the six cycles of VCAP-AMP-VECP was 19% (6/32) in the elderly group.

Maintenance oral chemotherapy

For some elderly patients treated with the VCAP-AMP-VECP regimen who had some response to the initial treatment, maintenance oral chemotherapy was administered after fewer than three cycles of the VCAP-AMP-VECP regimen, considering their quality of life and the difficulty in continuing the intensive regimen. We also evaluated the outcome of patients treated with maintenance oral chemotherapy.

Eleven out of 34 (32%) patients received maintenance oral chemotherapy. The disease status at the beginning of the maintenance therapy was CR in 2 patients, PR in 8 patients, and SD in 1 patient. In patients who received maintenance therapy, MST and OS at 2 years were 16.7 months and 32.7% (95% CI: 8.3-60.6%), respectively. Twenty three patients were not treated with the maintenance therapy, and the disease status was CR in 1 patient, PR in 12 patients, and PD in 3 patients, for the patients assessed after 3 cycles of VCAP-AMP-VECP, and PR in 1 patients and PD in 4 patients, for the patients who were treated no more than 2 cycles of the regimen. For the two remaining patients, it was not clear whether they were treated with maintenance therapy or not. The clinical characteristics of the patients according to the maintenance therapy are summarized in Table 3. There was not significant difference, except for the platelet count, in the background between the patients treated with the maintenance therapy and those without the treatment.

A simplified ATL-prognostic index (PI)

An ATL-PI has been proposed to develop a system for risk stratification in patients with acute- and lymphoma-type ATL [15]. A simplified ATL-PI was defined with five risk factors as follows: 2 (if stage = III or IV) + 1 (if ECOG PS >1) + 1 (if age >70 years) + 1 (if albumin <3.5 g/dL) + 1 (if sIL-2R >20,000 U/mL). Scores from 0 to 2 were categorized into the low-risk group, 3 and 4 into the intermediate-risk group, and 5 to 6 into the high-risk group. MSTs were reported to be 4.5, 7.0, and 16.2 months, and OS at 2 years were reported to be 6%, 17%, 37% for patients at high, intermediate, and low risk, respectively [15]. We evaluated the elderly patients in our study using the simplified ATL-PI. Ten patients were

excluded because of missing data. The MSTs were 5.1, 12.9, and 19.5 months, and OS at 2 years were 17.8% (95% CI: 3.4-41.4%), 18.4% (95% CI: 5.8-36.6%), and 50.0% (95% CI: 0.6-91.0%) for patients in the high-risk (n = 4), intermediate-risk (n = 23), and low-risk groups (n = 17), respectively (Figure 4a). We identified no statistically significant difference, but observed a tendency for a better prognosis in the low-risk group. The effects of the risk factors in the ATL-PI on OS in the elderly patients were analyzed with univariate analysis. The survival rate was significantly lower in patients with a lower Alb level [≥3.5 (n = 25) vs. <3.5 g/dL (n = 19); P = 0.047; log-rank test]] (Figure 4b). However, other factors, such as stage [I, II (n = 5) vs. III, IV (n = 39); P = 0.45], PS [0, 1 (n = 21) vs. 2-4 (n = 23); P = 0.29], and sIL-2R [≤20,000 (n = 29) vs. >20,000 U/mL (n = 15); P = 0.058] did not significantly affect OS.

Discussion

In this retrospective study, we showed the treatment outcome of elderly patients with aggressive ATL. In our hospital, the median ages of patients with aggressive ATL at diagnosis were 61 years between 1994 and 2000 (range: 33-84 years) and 65 years between 2001 and 2010 (range: 35-85 years). The rate of patients 70 years or older was 16% (9 out of 57) in the former period and 36% (45 out of 126) in the latter period (Figure 5). The age of ATL patients has increased over time in our hospital, similar to the tendency observed in a nation-wide survey [14]. Therefore, the best way to treat elderly ATL patients has become a very important issue.

The VCAP-AMP-VECP regimen has been reported to be more likely to benefit younger patients, because no difference was detected in the outcome between patients ≥56 years old treated with

VCAP-AMP-VECP and those treated with CHOP-14 [9]. In our study, for patients treated with VCAP-AMP-VECP, the MST and OS at 2 years were almost identical to these results in patients ≥56 years old but under 70 years old in a clinical trial [9]. On the other hand, those who received another treatment as the first choice had a poorer prognosis. Selection bias was included in the choice of treatment in this retrospective study. Patients treated with chemotherapy other than VCAP-AMP-VECP were older (P = 0.02; Mann-Whitney U test) and may have been in worse condition. In addition, patients who did not complete first cycle of VCAP-AMP-VECP were excluded from VCAP-AMP-VECP group in this retrospective analysis, and patients who became treatment-resistant extremely early after the start of chemotherapy may not have been included in the VCAP-AMP-VECP group. Thus, we cannot conclude the superiority of VCAP-AMP-VECP compared to other regimens. However, our result suggests that a nearly identical outcome to the younger patients may be expected in elderly patients receiving a VCAP-AMP-VECP-like regimen if they are in relatively good condition. Dose adjustment may be required for the VCAP-AMP-VECP-like regimen when treating elderly patients to reduce the adverse events, because hematologic toxicity and infections were reported more frequently with the VCAP-AMP-VECP regimen than with CHOP-14. Indeed, only 8.8% (3/34) of elderly patients were treated with a full dose of VCAP-AMP-VECP as the initial treatment in our study. The degree of dose reduction varied, and the doses were reduced to about half to 80% in most cases according to the patients' condition.

We should keep in mind that two-fifths of elderly patients were not candidates for an intensive treatment such as VCAP-AMP-VECP, even in our university hospital. The ratio of elderly

patients with a worse general condition who were not candidates for this intensive regimen may be higher at the local public hospital. Thus, further improvement in the treatment strategy for elderly ATL patients is required.

The total number of cycles of VCAP-AMP-VECP that constituted a complete treatment was defined as six or seven in the clinical study [8, 9]. In our study, only six out of 32 patients (19%) completed six cycles of VCAP-AMP-VECP, although some patients were treated with maintenance therapy as described below. Three of the patients who completed six cycles of the VCAP-AMP-VECP regimen survived over 2 years. Thus, continuation of intensive chemotherapy may contribute to prolonged survival. However, the rate of completion of six cycles of VCAP-AMP-VECP was only 32% even in the clinical study, mainly because of progressive cytopenia and PD during the treatment [9]. Thus, for some elderly patients who responded to VCAP-AMP-VECP, we stopped the intensive chemotherapy after two or three cycles and orally treated them with etoposide and/or sobuzoxane and/or prednisone as maintenance therapy. We cannot conclude the efficacy of maintenance therapy in this study, because the number of patients was not sufficient, and the background may be heterogeneous for patients treated with such a strategy. However, our results appeared to be acceptable, and such a treatment strategy may become an option with an emphasis on quality of life of elderly patients. Further examination is expected to confirm the efficacy of maintenance therapy.

Most elderly patients included in this study were at intermediate or high risk in the ATL-PI, which suggests that our study did not inadvertently select patients with a better disease status. We could

not show a significant difference in prognosis with the ATL-PI in our patients. The number of patients may have been too small to analyze the efficacy of the prognostic index. Furthermore, low-risk patients were rare among the elderly patients in our study. The fact that older age itself is included as a risk factor in the ATL-PI may be the main reason for the deviation in the risk group.

The efficacy of mogamulizumab, a humanized anti-CC chemokine receptor 4 antibody, as a single agent has been reported for relapsed ATL [17]. Mogamulizumab is now available in clinical practice for relapsed refractory ATL patients in Japan. Thus, for example, administration of mogamulizumab for maintenance therapy may prevent relapse or regrowth of the disease. On the other hand, a clinical trial for mogamulizumab combined with VCAP-AMP-VECP as the initial treatment for aggressive ATL has been performed, although the result has not been published yet. Thus, mogamulizumab with dose-reduced VCAP-AMP-VECP or a less toxic regimen as the initial treatment may become a treatment option for elderly patients with aggressive ATL in the near future. An appropriate clinical trial is warranted to reveal the efficacy of such an approach. However, a prospective clinical trial may be difficult in elderly patients with aggressive ATL. In this report, no patient was treated with mogamulizumab, and our results provide a basis for the treatment result in elderly patients before the introduction of antibody therapy for the treatment of ATL.

In conclusion, our results suggest that dose-modified VCAP-AMP-VECP may become an optional regimen for the treatment of elderly patients with aggressive ATL if their general condition is good enough for intensive chemotherapy. In addition, two or three cycles of VCAP-AMP-VECP followed

by maintenance therapy may also become a treatment option for elderly patients. However, the outcome is not good enough, and thus, further improvement in the treatment strategy is warranted.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Figure Legends

Figure 1. Flowchart of patients. Allo-HSCT, allogeneic hematopoietic stem cell transplantation

Figure 2. Survival of patients by age.

Figure 3. Survival of the elderly patients according to the initial therapy .

Figure 4. Survival of elderly patients. a, Survival according to the simplified ATL-prognostic index (PI).

b, Survival according to Albumin (Alb).

Figure 5. Age distribution of the patients with aggressive ATL at diagnosis.

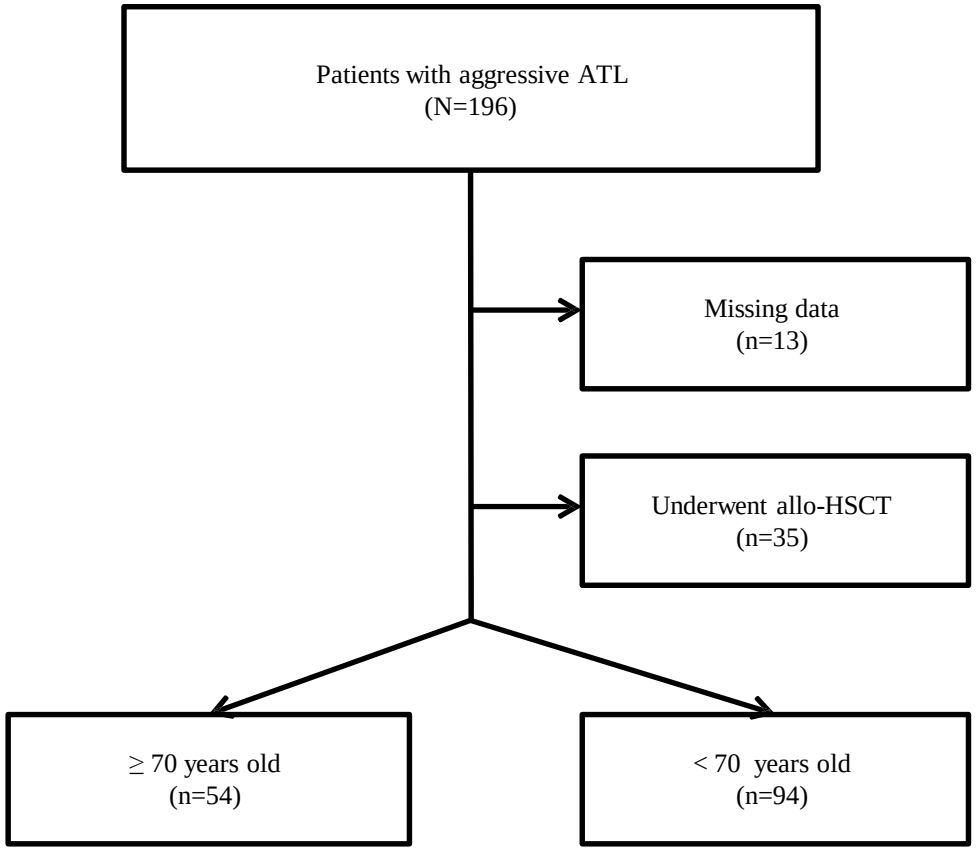
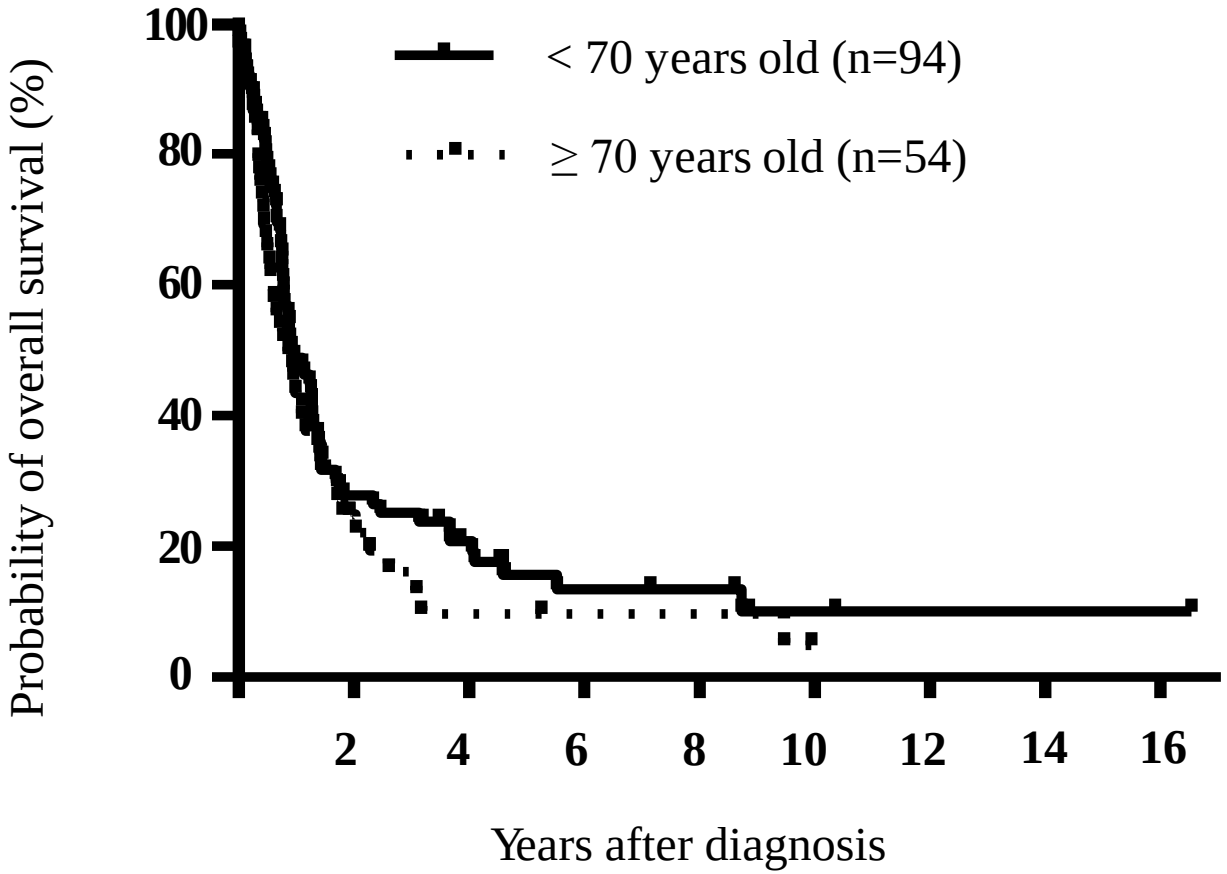
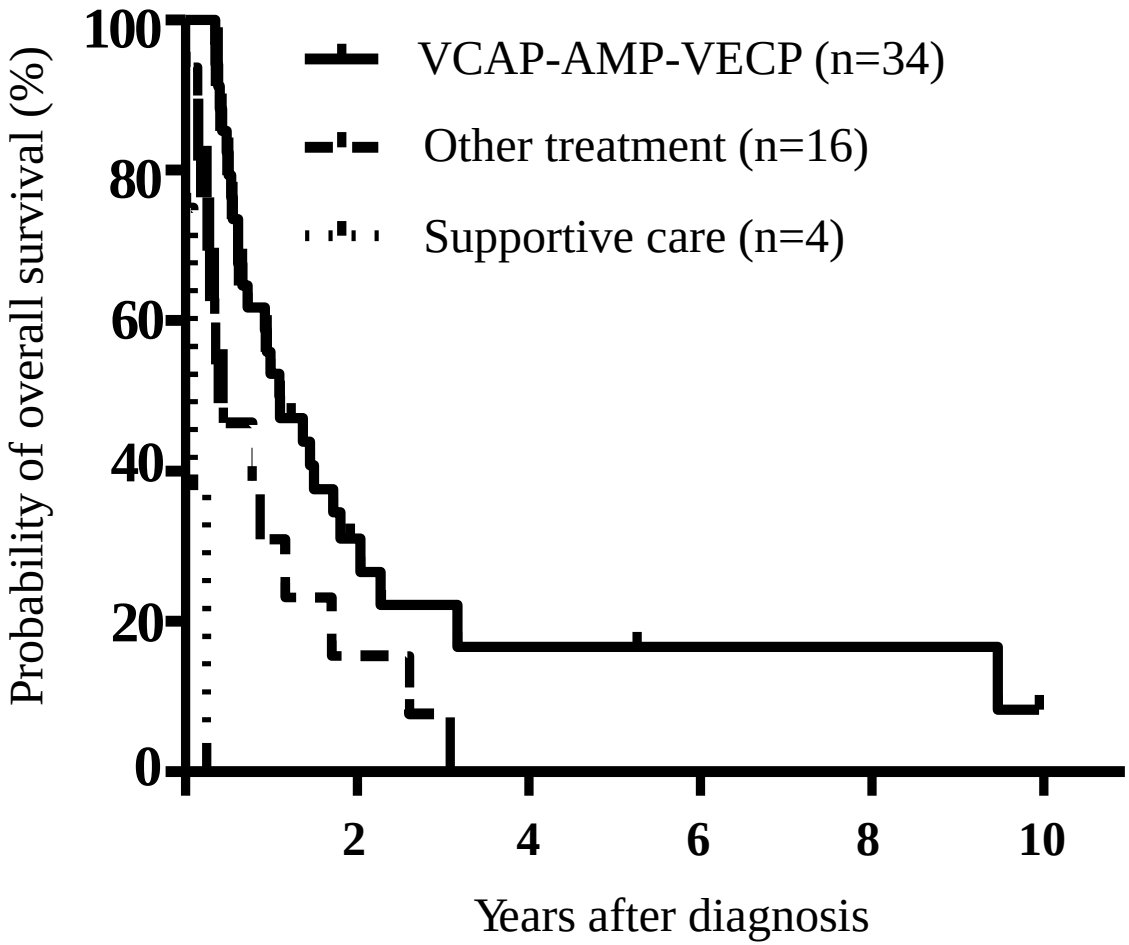


Figure 1. Flowchart of patients



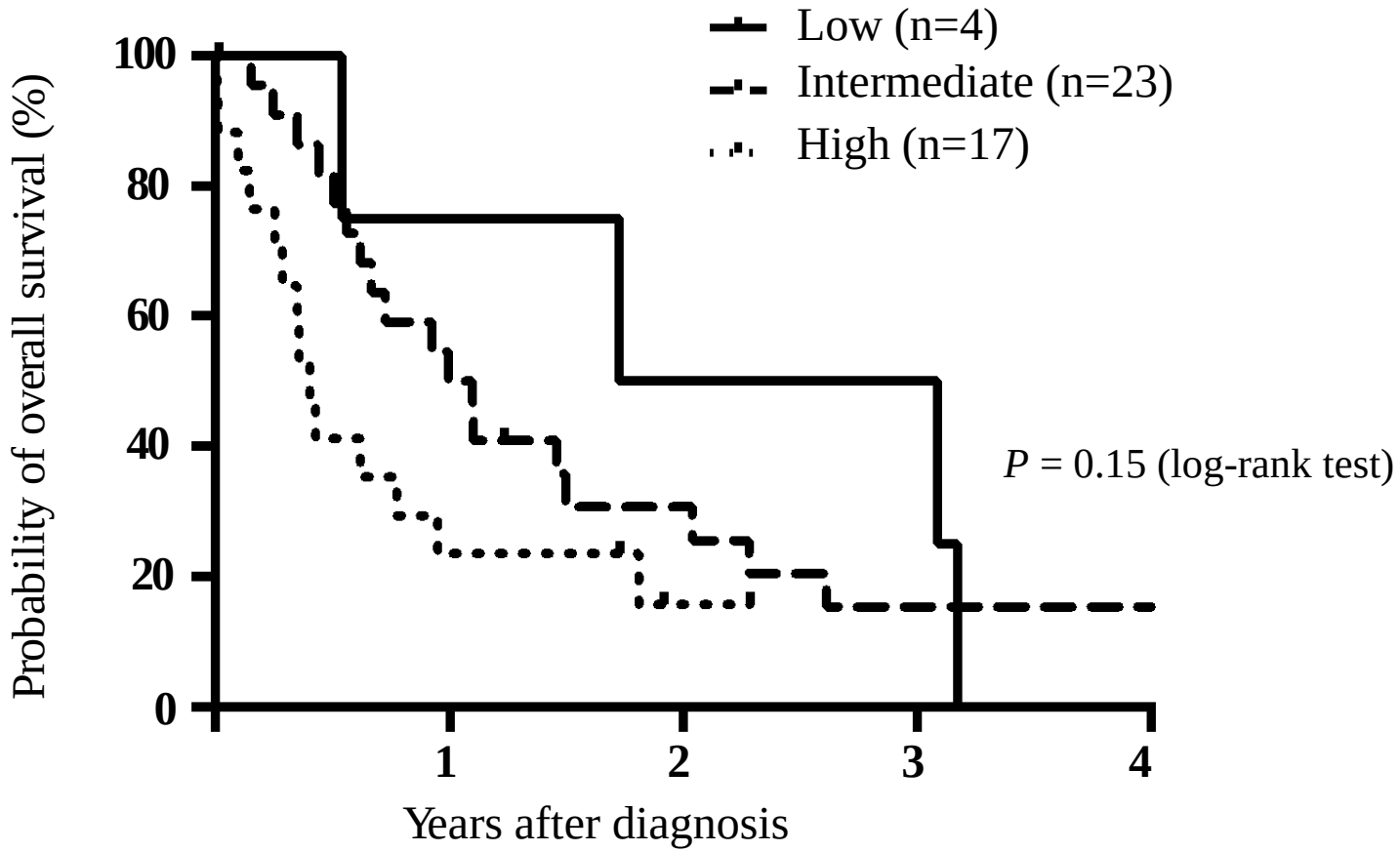
No. at risk									
< 70 years old	94	21	13	6	5	2	1	1	1
≥ 70 years old	54	9	3	2	2	0	0	0	0

Figure 2. Survival of patients by age



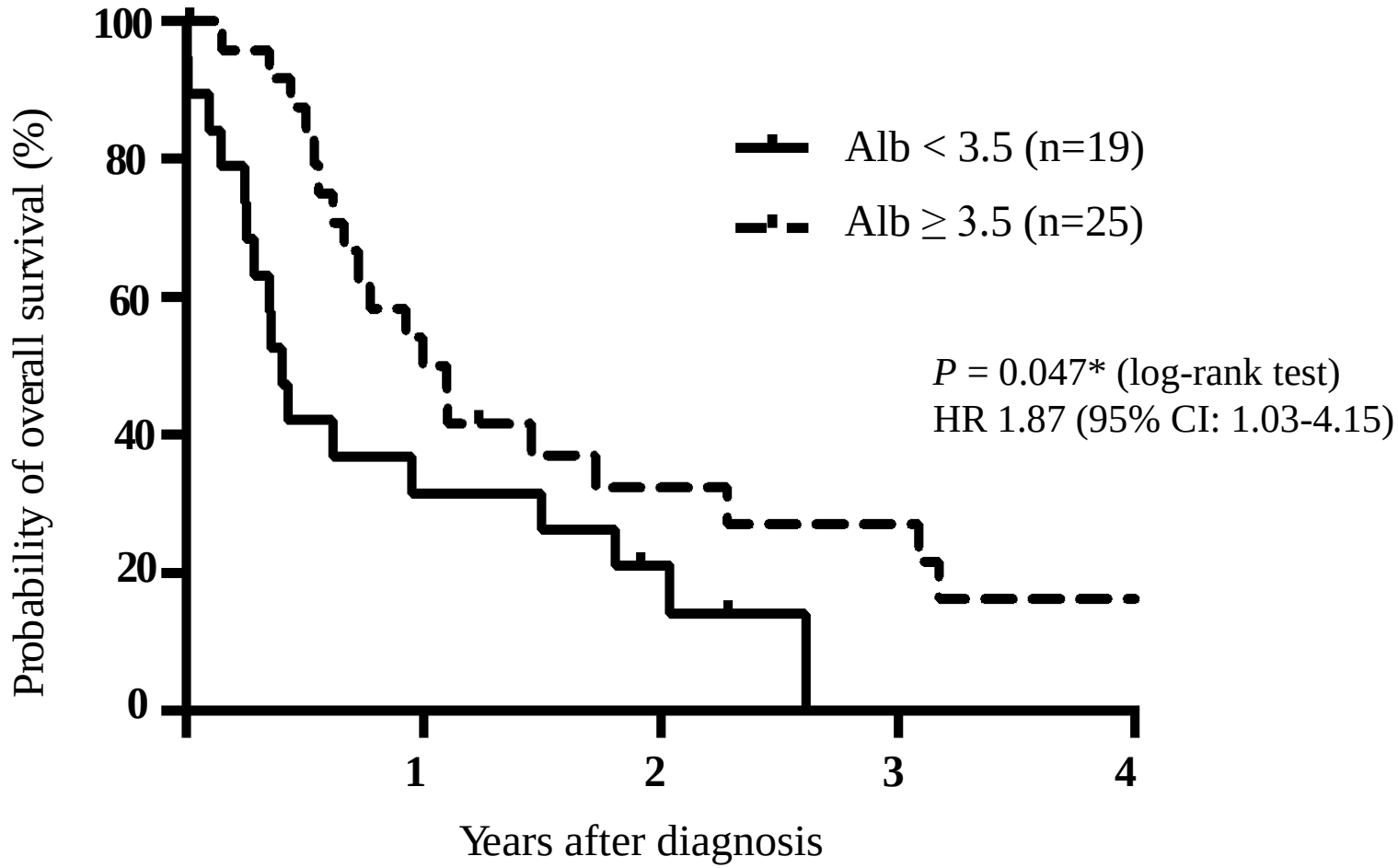
No. at risk						
VCAP-AMP-VECP	34	7	3	2	2	0
Other treatment	16	2	0	0	0	0
Supportive care	4	0	0	0	0	0

Figure 3. Survival of the elderly patients according to the initial therapy



No. at risk					
Low	4	3	2	2	0
Intermediate	23	11	6	3	3
High	17	4	1	0	0

Figure 4. Survival of elderly patients. a Survival according to simplified ATL-PI.



No. at risk					
Alb ≥3.5	25	12	6	5	3
Alb <3.5	19	6	3	0	0

Figure 4. Survival of elderly patients. b Survival according to Alb.

Figure 5. Age distribution of patients with aggressive ATL at diagnosis

Table 1. Characteristics of all patients with aggressive ATL

	< 70 years old (n=94)	≥ 70 years old (n=54)	*P* value
Median age (range) (year)	60.5 (34-69)	74 (70-85)	
Sex			1
Male	52	30	
Female	42	24	
Subtype			0.21
Acute type	76	38	
Lymphoma type	15	15	
Unfavorable chronic type	3	1	
WBC count ($\times 10^9$/L), median (range)	9.9 (1.4-224.8)	7.2 (1.2-186.0)	0.01*
Neutrophil count ($\times 10^9$/L), median (range)	5.8 (0.2-108.5)	4.1 (0-21.6)	0.008*
Total lymphocyte count ($\times 10^9$/L), median (range)	2.9 (0.3-206.8)	1.7 (0.4-169.3)	0.04*
Platelet count ($\times 10^9$/L), median (range)	204 (18-566)	188 (58-415)	0.66
Serum total protein (g/dL), median (range)	6.3 (4.1-7.9)	6.6 (4.4-8.8)	0.21
Serum albumin (g/dL), median (range)	3.6 (2.2-4.7)	3.7 (1.3-4.5)	0.82
LDH (IU/L), median (range)	496 (151-9165)	503 (138-4425)	0.46
BUN (mg/dL), median (range)	15 (5-57)	16 (5-81)	0.43
Soluble IL-2R (U/mL), median (range)	12252.5 (397-150124)	11212 (595-117784)	0.53
Serum corrected calcium (mg/dL), median (range)	9.9 (8.4-19.4)	9.8 (8.4-18.9)	0.85
Ann Arbor stage			0.5
I-II	5	5	
III-IV	89	49	
Performance status			0.85
0-2	67	40	
3, 4	27	14	
B symptom present	32	15	0.47
Initial treatment			< 0.0001*
VCAP-AMP-VECP (full dose)	47	3	
VCAP-AMP-VECP (dose modification)	16	31	
Other treatment	29	16	
Supportive care	2	4	

Table 2. Characteristics of elderly patients by initial treatment

	VCAP-AMP-VECP (n=34)	Other treatment (n=16)	Supportive care (n=4)
Median age (range) (year)	73 (70-85)	79 (70-84)	75.5 (72-85)
Sex			
Male	20	7	3
Female	14	9	1
Subtype			
Acute type	25	12	1
Lymphoma type	9	4	2
Unfavorable chronic type	0	0	1
WBC count ($\times 10^9$/L), median (range)	6.3 (3.0-186.0)	8.0 (1.2-27.9)	12.0 (8.1-17.1)
Neutrophil count ($\times 10^9$/L), median (range)	4.0 (0.3-21.6)	4.0 (0-12.1)	5.7 (2.9-10.1)
Total lymphocyte count ($\times 10^9$/L), median (range)	1.8 (0.3-169.3)	1.4 (0.5-23.7)	4.1 (0.6-13.2)
Platelet count ($\times 10^9$/L), median (range)	189 (58-415)	189 (101-339)	166 (111-293)
Serum total protein (g/dL), median (range)	6.7 (4.9-7.8)	6.3 (4.4-8.8)	6.5 (5.7-7.3)
Serum albumin (g/dL), median (range)	3.7 (1.3-4.5)	3.4 (2.7-4.1)	3.1 (2.7-4.3)
LDH (IU/L), median (range)	527 (176-4425)	526 (182-1634)	279 (138-1306)
BUN (mg/dL), median (range)	15 (5-47)	17 (11-81)	20 (18-22)
Soluble IL-2R (U/mL), median (range)	11931 (595-117784)	10981 (1171-29533)	10277 (3580-25136)
Serum corrected calcium (mg/dL), median (range)	9.8 (8.4-13.4)	9.7 (8.7-18.9)	9.8 (9.6-10.4)
Ann Arbor stage			
I-II	4	1	1
III-IV	27	15	3
Performance status			
0-2	27	11	2
3, 4	7	5	2
B symptom present	10	4	1

Table 3. Characteristics of elderly patients according to maintenance oral chemotherapy

	Maintenance oral chemotherapy (+) (n=11)	Maintenance oral chemotherapy (-) (n=21)	*P* value
Median age (range) (year)	73 (70-80)	74 (70-85)	0.90
Sex			1.00
Male	6	12	
Female	5	9	
Subtype			0.09
Acute type	6	18	
Lymphoma type	5	3	
WBC count ($\times 10^9$/L), median (range)	7.0 (3.3-36.3)	6.1 (3.0-186.0)	0.84
Neutrophil count ($\times 10^9$/L), median (range)	4.3 (0.3-6.9)	3.7 (0.6-21.6)	0.61
Total lymphocyte count ($\times 10^9$/L), median (range)	1.7 (0.5-26.8)	2.1 (0.4-169.2)	0.34
Platelet count ($\times 10^9$/L), median (range)	250 (123-415)	170 (58-365)	0.0122*
Serum total protein (g/dL), median (range)	7.0 (4.9-7.5)	7.0 (4.9-7.8)	0.31
Serum albumin (g/dL), median (range)	4.0 (1.3-4.1)	4.0 (2.7-4.5)	0.43
LDH (IU/L), median (range)	488 (203-938)	635 (176-4425)	0.66
BUN (mg/dL), median (range)	15 (5-38)	14 (10-47)	0.49
Soluble IL-2R (U/mL), median (range)	5752 (940-39734)	12223 (595-117784)	0.58
Serum corrected calcium (mg/dL), median (range)	10.0 (9.0-12.8)	10.0 (8.4-13.4)	0.86
Ann Arbor stage			1.00
I-II	1	3	
III-IV	10	18	
Performance status			1.00
0-2	9	16	
3, 4	2	5	
B symptom present	5	5	0.25