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Original Article

Treatment of Hodgkin's Disease: A Twenty-Year Follow-up of Patients at a Center in Korea

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Hodgkin's disease (HD) is a hematologic malignancy which shows common features regardless of race, but racial differences may be considered with certain clinical characteritcs. HD in Korea shows somewhat different characteristics when compared to cases in Western countries. We evaluated the clinical and histopathologic characteristics of HD, the outcomes of various chemotherapy regimens, and prognostic factors of HD in Korea. One hundred and five patients with initial histopathologic diagnosis of Hodgkin's disease were retrospectively reviewed 20 years after diagnosis at Yonsei University College of Medicine. Nodular sclerosis was the most common histopathogic subtype (41%) and mixed cellularity was nearly as common (40%). The overall complete remission rate (CR) was 87.6%. The disease-free survival (DFS) and overall survival (OS) rate were 79.2% and 84.8% at 5-years, 70% and 79.2% at 10- and 20-years. There were no significant differences in CR rate and DFS, but OS rates were significantly higher in m-BACOP and ABVD regimen. Univariate analysis revealed that age, B-symptom, ECOG scale, Ann Arbor stage, international prognostic index, and serum β_2-microglobulin level were significant prognostic factors for both DFS and OS. Multivariate analysis demonstrated that age, B symptoms, and ECOG scale were significant prognostic factors for OS only. In conclusion, the survival rates of HD patients in our center were superior to those of previous reports in Korea and Western countries. Considering the higher OS rate and decreased incidence of side effects, the ABVD regimen may be recommended for the initial treatment of Hodgkin's disease.

Key Words: Hodgkin's disease, twenty year survival, chemotherapy, Korea

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INTRODUCTION

Hodgkin's disease (HD) is often considered a curable disease since the chemotherapy combination MOPP (mechlorethamine, vincristine, procarbazine, and prednisolone) was introduced by De Vita et al.[1] De Vita and colleagues achieved a 50% cure rate for advanced-stage HD patients using this regimen. After the initial success of the MOPP regimen, many combination chemotherapies were introduced that improved survival rate and reduced complications. Combinations such as BCVPP (bleomycin, cyclophosphamide, vincristine, procarbazine, and prednisone) or ChlVPP (chlorambucil, vinblastine, procarbazine, and prednisone) have also been used with some success. However, outcomes were not significantly improved until the ABVD (doxorubicin, bleomycin, vincristine, and dacarbazine) regimen was introduced in 1975 by Bonadonna and colleagues.[2] The MOPP-ABV (cyclophosphamide, vincristine, procarbazine, prednisone, doxorubin, bleomycin, and vinblastine) hybrid regimen was tried in 1982 by Vancouver group,[3] and BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, and procarbazine) was introduced by the German Hodgkin Study Group in 1993.[4] The ABVD or BEACOPP regimen was generally found to be superior to the others, especially in advanced cases.[5,6]

HD in Korea shows somewhat different characteristics when compared to cases in Western countries. However, there were few studies of long-term survival and few studies that compared the results of various chemotherapy regimens. Using a twenty-year follow up, this study aimed to evaluate clinical and histopathological charac-

teristics, therapeutic outcomes of chemotherapy regimens, and prognostic factors of HD.

MATERIALS AND METHODS

Patients

One hundred five patients with an initial histopathologic diagnosis of HD were retrospectively reviewed. These patients had been diagnosed at the Yonsei University College of Medicine from January 1985 to February 2005. The median follow up duration was 83 (6-241) months.

Diagnosis and staging

A tissue biopsy was performed in all patients for diagnostic purposes. The patients were classified according to the Rye histopathologic classification, which included measures of lymphocyte predominance (LP), nodular sclerosis (NS), mixed cellurarity (MC), and lymphocyte depletion (LD).

The Ann-Arbor staging system was used in this study. Staging modalities were computed using one of the following methods: tomographic scan of the neck, chest, abdomen and pelvis, whole body bone scan, gallium scan, positron emission tomography (PET) scan, or bilateral bone marrow aspiration with biopsy. Initial lactate dehydrogenase (LDH), β_2-microglobulin, erythrocyte sedimentation rate (ESR), and albumin level were measured. We used the LDH index because the LDH upper normal value changes over time depending on the method of measurement. The LDH index is the ratio of patient's LDH level and upper normal LDH level at that time.

Treatment

The patients were divided into 3 groups depending upon the initial treatment modality: radiation alone, chemotherapy alone, and combined chemo-radiotherapy. The chemotherapy regimens used were C-MOPP (cyclophosphamide, vincristine, procarbazine, prednisone), ABVD, COPP-ABV hybrid (cyclophosphamide, vincristine , procarbazine, prednisone, doxorubin, bleomycin, and vinblastine), m-BACOP (methotrexate, bleomycin, adriamycin, cyclophosphamide, vincristine, prednisolone) and other regimens.

Criteria for response

Therapeutic response was defined based on the WHO criteria. Complete response (CR) was defined as the disappearance of all clinical evidence of lymphoma by physical examination and restaging work-up and no histologic evidence of lymphoma if it had been found earlier on bone marrow or spinal fluid examination. Partial response (PR) was defined as a greater than 50% reduction of the diameter of measurable tumor lesions for at least 4 weeks. Stable disease was defined as less than 50% response without progression of disease. Progressive disease (PD) was defined as 25% increase in diameters of known lesions or any sites of disease. Those with stable or progressive disease were deemed to have no response (NR).

Statistics

Comparison of characteristics was made using a chi-square (χ^2) test for the binary variables and a Mann-Whitney test for the continuous variables. The logistic regression was used to test the relationship between continuous variables and survival. The disease-free survival (DFS) and overall survival (OS) probabilities were calculated using the Kaplan-Meier method. Univariate association between the clinical features and DFS or OS was determined by the log-rank test. Multivariate analysis was used to test for the independent prognostic significance of variables using the Cox proportional hazards regression model. A p-value < 0.05 was used to indicate statistical significance. All calculations were performed using the SPSS software, version 11.0.1 (SPSS Inc, Chicago, IL, USA).

RESULTS

Patient characteristics

A total of 105 adults with newly diagnosed HD

were enrolled in this study. Males were affected more often than females (1.84 : 1), and the median age of patients was 35 years (range, 5 to 88 years). The clinical characteristics of the patients are shown in Table 1.

Nodular sclerosis was the most common histopathogic subtype (41%) and the mixed cellularity (40%) was nearly as common. Eighty-six patients (81.9%) were beyond stage I according to the Ann-Arbor staging system.

Table 1. The Characteristics of 105 Patients

Clinical parameters	No.	(%)
Age (yr) median [range]	35	5 - 88
Sex (M/F)	68/37	64.8/35.2
ECOG		
0 or 1 vs. ≥ 2	94/11	(89.5/10.5)
Serum lactic dehydrogenase index		
≤ 1 × normal vs. > 1 × normal	52/30	(49.5/28.6)
NA	23	(21.9)
Albumin (g/dL)		
≤ 3.5 vs. > 3.5	21/74	(20.0/70.5)
NA	10	(9.5)
ESR		
≤ 1 × normal vs. > 1 × normal	60/45	(57.1/42.9)
β_2-microglobulin		
≤ 1 × normal vs. > 1 × normal	45/20	(42.9/19.0)
NA	40	(38.1)
International prognostic index		
Low	65	(61.9)
Low intermediate	22	(21.0)
High intermediate	11	(7.3)
High	7	(7.3)
Histopathologic subtypes		
Lymphocyte predominance	13	(12.4)
Nodular sclerosis	43	(41.0)
Mixed cellularity	42	(40.0)
Lymphocyte depletion	7	(6.7)
Stage		
I	19	(18.1)
II	44	(41.9)
III	19	(18.1)
IV	23	(21.9)

NA, not assessed; ECOG, Eastern Cooperative Oncology Group; ESR, erythrocyte sedimentation rate.

Table 2. Presenting Symptoms and Signs

Clinical presentation	No. (%)
Lymphadenopathy	94 (89.5)
Cervical	79 (75.2)
Mediastinal	6 (5.7)
Axillary	5 (4.8)
Inguinal	3 (2.9)
Paraaortic	1 (1.0)
B symtoms	31 (29.5)
Other Symptoms*	6 (5.7)
Total	105 (100)

*Cough (2), both leg edema (2), both foot tingling sensation (1), both leg pain (1), jaundice (1), right upper quadrant pain (1), dyspnea (1), left arm pain (1).

The most common presenting symptom at the time of diagnosis was lymphadenopathy (89.5%). Cervical lymphadenopathy was the most common type (75.2%). B symptoms were present in 29.5% of the patients (Table 2).

The median follow-up duration was 53 months for DFS and 59 months for OS.

Therapeutic outcomes

Therapeutic modalities used in this study are summarized in Table 3. Radiotherapy alone was used in 34 patients, chemotherapy alone in 38 patients, and combined chemo-radiotherapy in 33 patients. Of the 34 patients who received radiotherapy, 33 patients had stage I or II disease and 1 had stage III. Of the 63 patients with stage I or II disease and 41 patients with stage III disease, 30 received chemotherapy. Radiotherapy was added for patients who had a bulky mass or who showed suspicious residual lesions after chemotherapy. In 71 patients with chemotherapy and combined chemo-radiotherapy, the COPP-ABV hybrid regimen was used in 29 patients (40.8%), and ABVD regimen in 19 patients (26.8%).

Complete response (CR) was achieved in 92

Table 3. Initial Responses According to the Therapeutic Modalities

	RTx	CTx	CTx + RTx	*p* value
CR	31/34 (91.2%)	29/38 (76.3%)	32/33 (97.0%)	0.489
Relapse	14/31 (45.2%)	2/29 (6.9%)	2/32 (6.3%)	< 0.0001*

*between RTx and other two groups.
RTx, radiotherapy; CTx, chemotherapy; CTx+RTx, combined chemo-radiotherapy; CR, complete response.

Table 4. Initial Responses According to the Chemotherapeutic Regimens

	C-MOPP	ABVD	COPP-ABV	m-BACOP	*p* value
CR	11/13 (84.6%)	13/15 (86.7%)	23/27 (85.2%)	10/10 (100%)	0.844
Relapse	1/11 (9.1%)	1/13 (7.7%)	2/23 (8.7%)	0/10 (0%)	0.393

CR, complete response; C-MOPP, cyclophosphamide, vincristine, procarbazine, and prednisolone; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; COPP-ABV, cyclophosphamide, vincristine, procarbazine, prednisone, doxorubin, bleomycin, and vinblastine; m-BACOP, methotrexate, bleomycin, adriamycin, cyclophosphamide, vincristine, and prednisolone.

patients (87.6%). The CR rate was 91.2% in the radiotherapy group, 76.3% in chemotherapy group, and 97% in combined chemo-radiotherapy group ($p = 0.489$, Table 3). Among 92 patients who achieved CR, 18 patients had a recurrence of HD. The overall relapse rate was 17.4%, and the radiotherapy group showed significantly higher relapse rate than other two groups ($p < 0.0001$, Table 3). In the chemotherapy group and combined chemo-radiotherapy group, neither the CR rate nor the relapse rate was significantly different based upon which chemotherapeutic regimen was used (Table 4).

The DFS rate among the 92 patients who showed CR was 85.5% at 2-years, 79.2% at 5-years and 70.0% at 10- and 20-years (Fig. 1A). OS rate was 84.8% at 5-years and 79.2% at 10- and 20-years (Fig. 1B).

Fig. 2 shows the OS as it relates to the histologic subtypes (A) and stages (B). The OS rate after 10 years was significantly lower in those with lymphocyte depleted type disease than in the other subtypes ($p = 0.01$, 57.1% in LD vs. 76.6% in NS, 80.8% in LP, and 84.6 in MC). The 5-year OS was

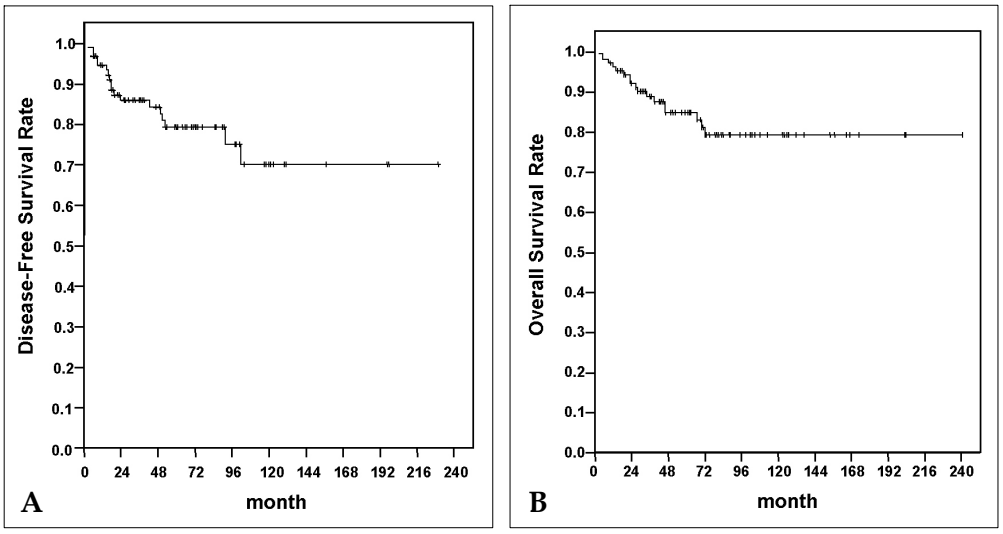

Fig. 1. Disease-free survival rate (A) and overall survival rate (B).

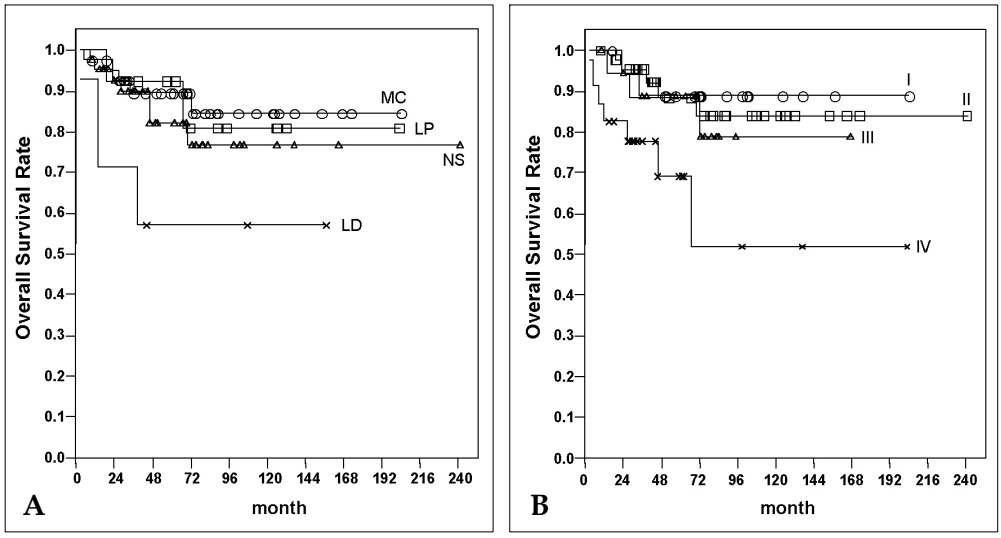

Fig. 2. (A) Overall survival rates according to the histological subtypes of the patients; LP, lymphocyte predominance; NS, nodular sclerosis; MC, mixed cellularity; LD, lymphocyte depletion. (B) Overall survival rates according to the Ann-Arbor stage.

88.9% in stage I, 88.3% in stage II, 78.7% in stage III, and 69.1% in stage IV. The OS rate was significantly decreased by the progression of stages ($p = 0.04$, Fig. 2B).

Relapse rate was 45.2% in the radiotherapy group, 6.9% in chemotherapy group, and 6.3% in combined chemo-radiotherapy group. Among 14 patients who relapsed in radiotherapy group, 6 patients had stage 1 disease and 8 had stage 2 disease, and the MC was the most frequent subtype (8 cases). In early stages (stage I and II), patients who received chemotherapy alone showed higher DFS rate than those who received radiotherapy alone but the difference was not statistically significant (Fig. 3A). The relatively high relapse rate of the radiotherapy group and the combined chemo- radiotherapy may be explained by poor prognostic factors found in the early stages of their disease. In advanced stages, there were no significant differences in DFS among the three treatment groups (Fig. 3B). Both 10- and 20-year DFS rate were 100% in m-BACOP, 90% in ABVD, 86.8% in COPP/ABV, and 90.9% in C-MOPP. The DFS rates did not differ significantly among the chemotherapeutic regimens (Fig. 3C).

Although there were no statistically significant differences in OS rates among the three different treatment groups, the combined chemo-radiotherapy group showed a higher OS rate than other two groups (Fig. 4A). In early stages (stage I and II), there were no significant differences in OS rate among the three treatment groups (Fig. 4B). In advanced stages, the patients who received combined chemo-radiotherapy showed a higher OS rate than those who received chemotherapy alone but the difference was not statistically significant (Fig. 4C). The 10- and 20-year OS rate were 100% in m-BACOP, 93.3% in ABVD, 76.6% in COPP/ABV, and 65.3% in C-MOPP. In chemotherapy or combined chemo-radiotherapy groups, the ABVD and m-BACOP regimen showed a better OS rate than the COPP-ABV hybrid or C-MOPP regimen (Fig. 4B), The OS rate of the patients with ABVD regimen was significantly higher than that of the patients who had the COPP-ABV hybrid regimen ($p = 0.03$). For the twenty-year follow-up period, 17 patients (16.2%) were deceased. The primary causes of death were disease progression (58.8%) and infectious complications (17.6%).

Prognostic factors

Many pretreatment features such as age, sex, B-symptom, extranodal involvement, stage, ECOG scale, serum LDH level, serum β_2-microglobulin level, serum albumin level, and international

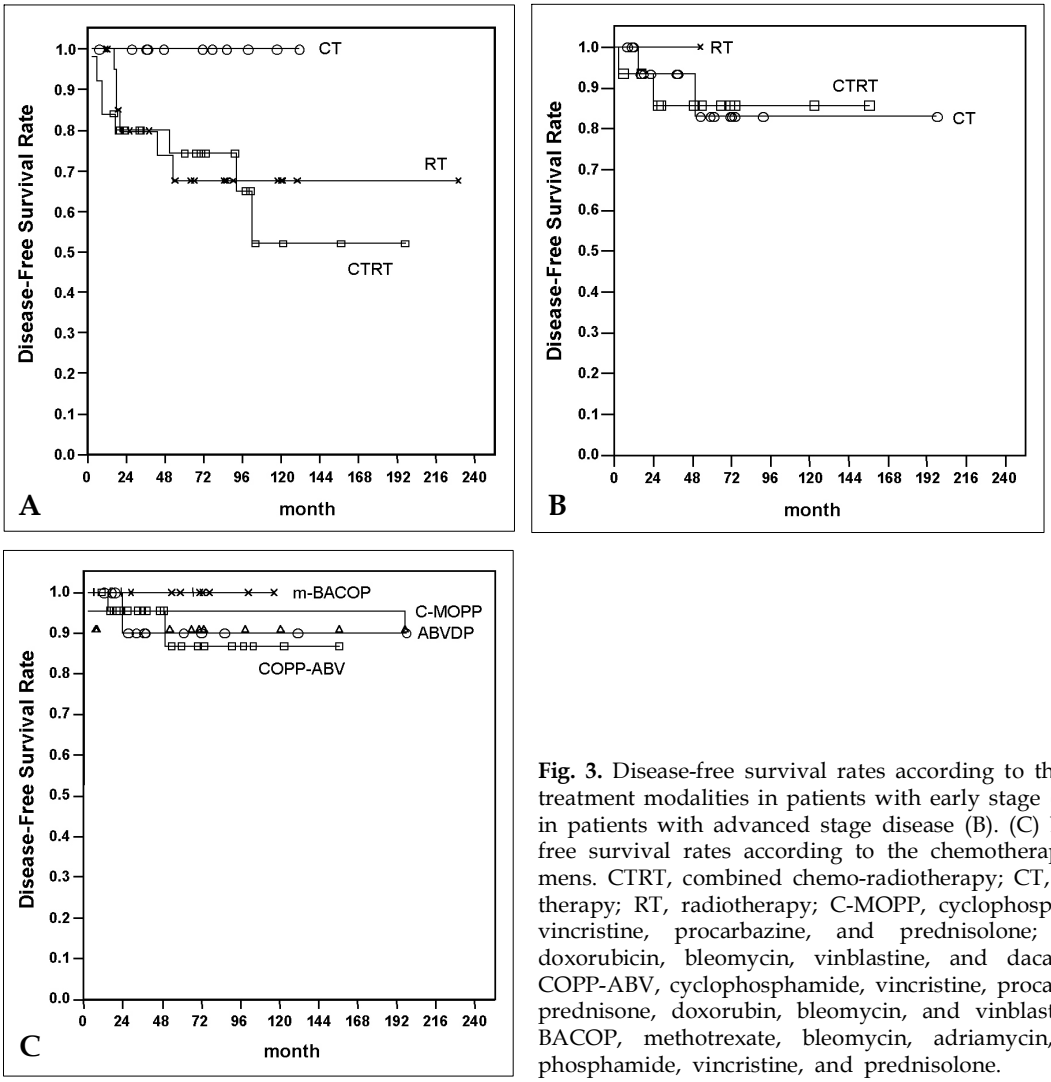

Fig. 3. Disease-free survival rates according to the initial treatment modalities in patients with early stage (A), and in patients with advanced stage disease (B). (C) Disease-free survival rates according to the chemotherapy regimens. CTRT, combined chemo-radiotherapy; CT, chemotherapy; RT, radiotherapy; C-MOPP, cyclophosphamide, vincristine, procarbazine, and prednisolone; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; COPP-ABV, cyclophosphamide, vincristine, procarbazine, prednisone, doxorubin, bleomycin, and vinblastine; m-BACOP, methotrexate, bleomycin, adriamycin, cyclophosphamide, vincristine, and prednisolone.

prognostic index were introduced as prognostic factors in HD.

In the current study, univariate analysis revealed that high ECOG scale (≥ 2) and β_2 microglobulin level consistently favored a poor prognosis for CR, DFS and OS. Old age (> 60), the presence of B symptom, advanced stage ($\geq$ III), high IPI and lymphocyte depletion subtypes also favored a poor prognosis for CR and OS, but not for DFS. LDH level was also a significant prognostic factor for CR (Table 5).

Multivariate analysis of covariates in the Cox regression model demonstrated that age, the presence of B-symptom, lymphocyte depletion subtypes, and ECOG scale remained as independent prognostic factors for CR and OS (Table 6).

DISCUSSION

Hodgkin's disease, firstly described by Sir Thomas Hodgkin in 1832, is a lymphoid tumor that represents 1% of all de novo malignancies occurring yearly, worldwide. Although patients with advanced stages of HD were considered incurable until the middle of the 20th century, there have been great strides in the management of HD due to the availability of effective chemotherapy regimens, the use of combined chemoradiotherapy with field irradiation in patients with early-stage disease, the introduction of effective salvage treatment with peripheral blood stem cell transplantation for relapse HD, a better understanding of prognostic factors, and a more sensi-

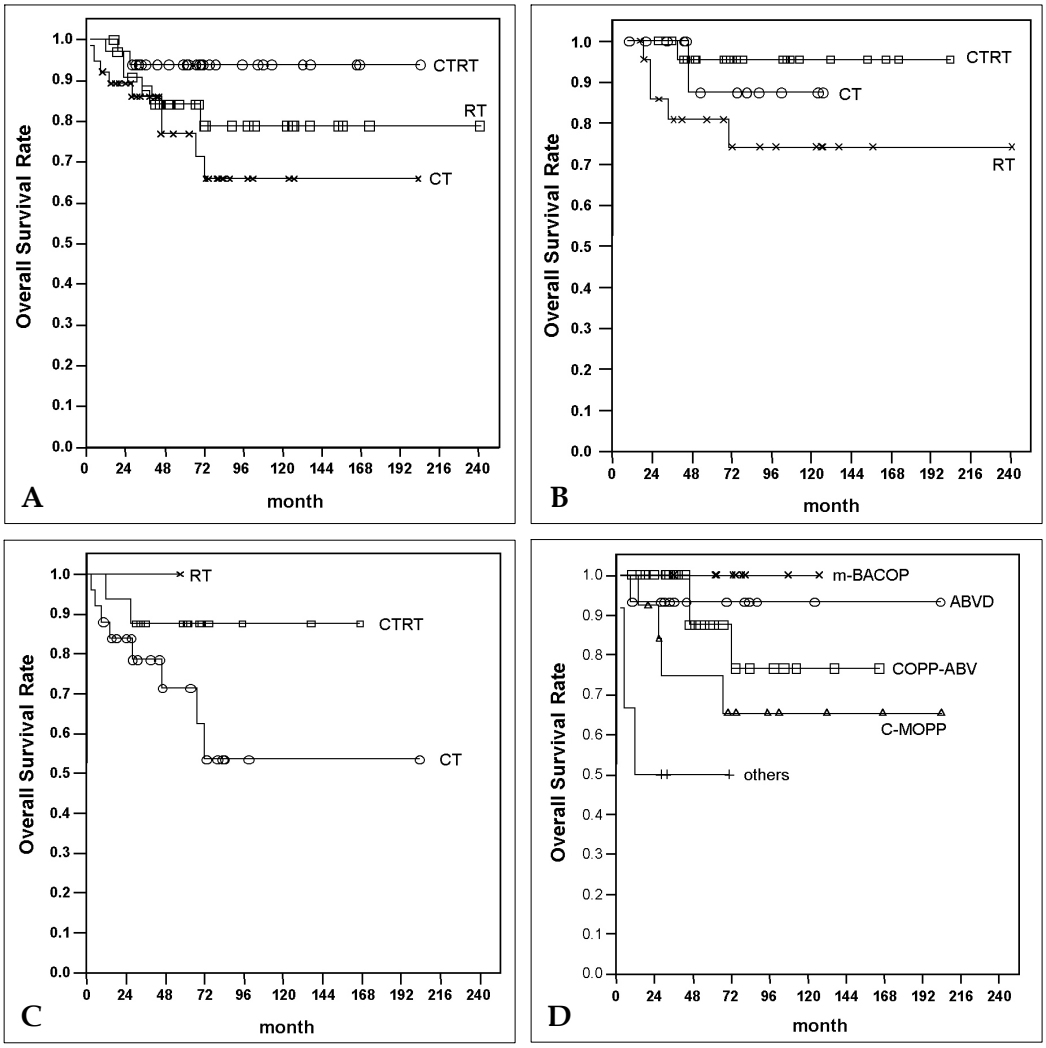

Fig. 4. Overall survival rates according to the initial treatment modalities in the total population (A), in patients with early stage (B), and in patients with advanced stage disease (C). (D) Overall survival rates according to the chemotherapy regimens. CTRT, combined chemo-radiotherapy; CT, chemotherapy; RT, radiotherapy; C-MOPP, cyclophosphamide, vincristine, procarbazine, and prednisolone; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; COPP-ABV, cyclophosphamide, vincristine, procarbazine, prednisone, doxorubin, bleomycin, and vinblastine; m-BACOP, methotrexate, bleomycin, adriamycin, cyclophosphamide, vincristine, and prednisolone.

tive realization of latetreatment-related morbidity.

HD in Korea shows somewhat different characteristics when compared with cases in Western countries. The incidence of Hodgkin's disease among all malignant lymphomas was 35-50% in Western countries, and 8.6-17.8% in Korea.[4-9]

According to the literature, mixed cellulariy is the most frequent histologic type in HD.[7,9,10] Park et al. reported in 1999 that mixed cellularity is found in 38% of cases and nodular sclerosis is found in 28%.[10] In this study, nodular sclerosis subtype (41%) had slightly higher incidence than mixed cellularity (40%), and It presented with different clinical characteristics compared to several previous studies. This change in subtypes of HD in Korea may be interpreted as a westernized phenomenon of HD.

Ryoo et al. and Ahn et al. reported 71.4% and 82% CR rate and a 59% and 66.6% of 5-year survival rate, respectively.[11,12] Park et al. reported a 72.9% 3-year survival rate in 39 patients.[10] In the current study, the overall CR rate in response of the initial therapy was 87.6%. The DFS and OS

Table 5. Univariate Analysis of Patients Characteristics for Complete Remission, Disease-Free Survival, and Overall Survival

Characteristics	CR		DFS		OS	
	Rate (%)	*p* value	Rate (%)	*p* value	Rate (%)	*p* value
Age ($\leq$ 60 vs. > 60, yrs)	81.7 vs. 30.8	< 0.001	73.2 vs. 51.4	0.1169	84.6 vs. 19.2	< 0.001
Male vs. Female	76.6 vs. 75	0.508	77.7 vs. 61.8	0.0556	78.2 vs. 75.9	0.717
B symptom*	61.8 vs. 81.9	0.021	79.5 vs. 68.9	0.8364	67.6 vs. 90.9	0.029
Extranodal Involvement*	67.6 vs. 79.5	0.130	91.6 vs. 66.2	0.2088	75.2 vs. 88	0.0895
Stage (I/II vs. III/IV)	86.6 vs. 62	0.002	85.3 vs. 66.3	0.2807	87.2 vs. 60.8	0.0092
ECOG (0-1 vs. 2-4)	83.5 vs. 21.4	< 0.001	74.3 vs. 34.3	0.0054	85.5 vs. 23.6	< 0.001
Serum LDH index†	86.8 vs. 71.4	0.011	60.4 vs. 87.4	0.3714	89.6 vs. 75.2	0.1476
β_2-microgobulin†	87.5 vs. 52.2	0.002	87.1 vs. 56.4	0.0046	94.1 vs. 44.4	< 0.001
Albumin ($\leq$ 3.5 vs. > 3.5 g/dL)	72.7 vs. 79.7	0.327	86.3 vs. 77.2	0.7159	76.7 vs. 81.9	0.2824
IPI		0.001		0.361		< 0.001
Low	89.5		69		93.7	
Low intermediate	73.1		82		76.9	
High intermediate	45.5		29.6		51.9	
High	25		20.2		18.8	
Histopathologic subtype		0.001		0.354		0.033
LP	100		92.3		84.6	
NS	83.7		75		83.7	
MC	95.2		80		88.1	
LD	57.1		100		57.1	

CR, complete response; DFS, disease-free survival; OS, overall survival; LDH, lactic dehydrogenase; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; LP, lymphocyte predominance; NS, nodular sclerosis; MC, mixed cellularity; LP, lymphocyte depletion.
*Present vs. Absent.
† $\leq$ 1 vs. > 1 × normal.

rate were 85.8% and 88.8% at 3 years, 79.2% and 84.8% at 5 years, and 70% and 79.2% from 10 to 20 years. According to the accumulated experience of Western countries, the CR rate ranged from 73-92%, and the OS rate varies from 80% to 89% at 5 years.[1,13] Compared with other studies in Korea, this study, which contains the largest number of enrolled patients and the longest follow-up duration, showed better CR, DFS, and OS rates, and results comparable to those of Western countries.

The chemotherapy regimens used to treat HD vary, as do the outcomes. Ahn et al. reported an 82% CR rate and a 66.6% 5-year survival rate in 28 patients using the COPP/ABV hybrid regimen.[12] Jung et al. reported that 71.4% patients achieved CR and 50.3% of patients achieved 5-year survival among 28 patients with the C-MOPP regimen.[14] Longo et al. reported that, among the complete response group, 64% cases were disease-free and the overall survival rate was 48% in a 20-year follow-up study of MOPP therapy.[15] Morgenield et al. reported that 66% of cases achieved CR and had a 48-month median survival time in COPP combined chemotherapy regimens.[16] Bonaddona et al. developed the ABVD

Table 6. Multivariate Analysis of Prognostic Factor

Factors	CR	DFS	OS
Age ($\leq$ 60 vs. > 60, yrs)	0.007	0.431	0.005
B symptom (present vs. absent)	0.049	0.528	0.008
ECOG (0 - 1 vs. 2 - 4)	0.006	0.093	< 0.001
Stage (I/II vs. III/IV)	0.048	0.155	0.086
Histopathologic subtypes	0.033	0.071	0.005
IPI (L, LI, HI, H)	0.360	0.640	0.572
Serum albumin ($\leq$ 1 vs. > 1 × normal)	0.892	0.494	0.271
ESR ($\leq$ 1 vs. > 1 × normal)	0.775	0.945	0.408

CR, complete response; DFS, disease-free survival; OS, overall survival; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; L, low; LI, low-intermediate; HI, high-intermediate; H, high; ESR, erythrocyte sedimentation rate.

regimen and reported that the results of ABVD alone or an alternating regimen of MOPP and ABVD were similar to the MOPP regimen.[17-19] Glick et al. reported that the MOPP/ABV hybrid regimen was superior to the sequential MOPP-ABVD regimen.[20]

In the current study, chemotherapy with various regimens was performed in 81 cases, and the therapeutic outcomes were different depending on the chemotherapy regimens. The ABVD regimen had a 86.7% CR rate and a 93.3% 5-year OS rate. The COPP/ABV hybrid regimen showed an 85.2% CR rate and an 87.5% 5-year OS rate. The C-MOPP regimen showed a 84.6% CR rate and a 65.3% 5-year OS rate. The 20-year rates of DFS and OS respectively, as with the 10-year, were 90% and 93.3% in ABVD, 76.6% and 86.8% in COPP/ABV, and 65.3% and 90.9% in C-MOPP. The OS rate of patients with the ABVD regimen was significantly higher than that of patients with the COPP-ABV hybrid regimen ($p = 0.03$). All of these survival rates were superior to those found among previous reports in Korea, and even those of Western reports.[17-21]

Among the various chemotherapy regimens, the ABVD regimen was deemed superior overall. These results were similar to those of Bonaddona et al.[17-19] According to a recent report by Bonaddona, after a median follow-up of 25 years, freedom from progression was found in 46% of patients after MOPP and 58% after ABVD, suggesting a relative reduction of approximately 30% favoring the ABVD arm. For both treatment regimens, the vast majority of failures were observed during the first 5 years of chemotherapy, and no deaths caused by progressive lymphoma were documented after 12 years from starting either MOPP or ABVD.[21] Therefore, ABVD regimen with or without radiotherapy is recommended as the treatment of choice for HD. ABVD regimen has lower side-effect incidence of azospermia (less than 20%) or prolonged amenorrhea (fewer than 5%)[22] and a lower risk of inducing secondary leukemia or myelodysplastic syndrome[21] as well as greater therapeutic potency.

According to recent Western reports, the role of newer and more intensified combined treatment regimens such as escalating BEACOPP have been emphasized,[23] but these still have a higher risk of treatment-related complications and need to be evaluated by large-scale randomized studies with long-term follow up.

In previous studies of Hodgkin's disease, various pretreatment factors were associated with therapeutic outcomes. Alessandro et al. reported that CR rate was significantly associated with histologic type and ERC (early response to chemotherapy),[24] and other studies in Western countries reported that age, ESR, histopathologic subtype, and mediastinal lymph node involvement could influence therapeutic outcomes.[25-27] Park et al. reported that age, performance status, serum albumin level, and serum LDH level were signifi-

cant prognostic factors when evaluated by univariate analysis, but multivariate analysis showed that only performance status was a statistically significant prognostic factor.[10] Hahn et al. reported that there is no significant prognostic factor in Hodgkin's disease among Korean people.[9]

In our study, univariate analysis revealed that high ECOG scale (≥ 2) and β_2-microglobulin level were significant factors of a bad prognosis for CR, DFS, and OS. Old age (> 60), the presence of B symptom, advanced stage (≥ III), high IPI, and lymphocyte depletion subtypes were poor prognostic factors for CR and OS though not for DFS. LDH level was an additional prognostic factor for CR (Table 5).

Multivariate analysis of covariates in the Cox regression model demonstrated that age, the presence of B-symptom, lymphocyte depletion subtypes, and ECOG scale remained independent prognostic factors of CR and OS (Table 6).

According to our study, ABVD regimen with or without radiotherapy might be considered the treatment of choice for HD because of the superior long-term survival benefit. Although the analysis about complications of treatment in relation to the various chemotherapy regimens was not performed, the ABVD regimen is recommended in the treatment for Hodgkin's disease due to the relatively low incidence of infertility and leukemogenic risk. Furthermore, continuous long-term follow-up will be needed to evaluate long term complications of each chemotherapy regimen.

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