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Autografting for Hodgkin's disease

Lymphocyte recovery as a positive predictor of prolonged survival after autologous peripheral blood stem cell transplantation in T-cell non-Hodgkin's lymphoma

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Summary:

We performed a retrospective study on recovery and survival of patients with T-cell NHL after autologous peripheral blood stem cell transplantation (APBSCT). Of a total of 39 patients with high-risk T-cell NHL, 33 were analyzed. Six patients who experienced early treatment mortality without full lymphocyte recovery were excluded. We chose absolute lymphocyte count (ALC) recovery as 1000 cells/μl as a cutoff value. ALC recovery day was defined as the first of 3 consecutive days with ALC above 1000 cells/μl. Univariate analysis revealed that age younger than 45 years, good international prognostic index, chemosensitive disease prior to APBSCT, and early ALC recovery (1000 cells/μl within 25 days of APBSCT) were predictors of prolonged survival. Multivariate analyses confirmed that chemosensitive disease prior to APBSCT and early ALC recovery were strongly associated with better overall survival (OS) ($P = 0.005$ and 0.011, respectively) and progression-free survival (PFS) ($P < 0.001$ and $P = 0.013$, respectively). Our finding, that ALC recovery $\geqslant$1000 cells/μl is an independent predictor of OS and PFS in T-cell NHL after APBSCT, suggests that earlier immune recovery may contribute to longer survival.
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Autologous stem cell transplantation (ASCT) is a standard therapeutic modality for multiple myeloma (MM) and relapsed chemotherapy-sensitive non-Hodgkin's lymphoma (NHL),[1,2] but not for metastatic breast cancer (MBC).[3,4] The main limitation of ASCT is the high relapse rate. Because graft-versus-tumor (GVT) effect is thought to lower relapse, there has been increasing interest in immune reconstitution following ASCT.[5] In support of this, it was recently shown that there is a relationship between lymphocyte recovery and relapse rate or survival in acute myeloid leukemia (AML), MM, NHL, and MBC,[6–8] suggesting that early lymphocyte recovery associated with immune reconstitution may act against the progression of residual disease. The prognostic implication or immunologic impact of lymphocyte recovery may be dependent on disease type or clinical subgroup.

Besides bone marrow (BM), peripheral blood (PB) is a common source of stem cells (SCs). BM stem cells (BMSCs) and PB stem cells (PBSCs) were found to differ in their ability to induce early lymphocyte recovery,[7] making it unclear if the absolute lymphocyte count recovery after ASCT is dependent on SC source. We wished to determine whether lymphocyte recovery reflects the reconstitution of immunologic function, as well as whether early lymphocyte recovery is predictive of prolonged survival. In addition, absolute lymphocyte count (ALC) has been shown to vary from day to day after ASCT. Thus, rather than measuring ALC at one point in time, we measured ALC on 3 consecutive days to evaluate the duration of ALC recovery.

In most previous studies of ALC recovery in NHL, the majority of treated patients have had B-cell NHL. There are few data for the clinical course of recovery in patients with T-cell NHL, primarily because of the relatively low incidence of T-cell NHL, as well as its histological heterogeneity. Thus, the possibility exists that the prognostic significance of ALC in patients with T-cell NHL may differ from that in patients with B-cell NHL. We therefore undertook a retrospective analysis of patients with T-cell NHL who underwent autologous peripheral blood stem cell transplantation (APBSCT) in order to evaluate the prognostic significance of ALC recovery.

Patients and methods

Patient populations

From March 1993 to December 2002, 39 patients with T-cell NHL underwent APBSCT at Asan Medical Center. All patients' data were collected prospectively and stored in a computerized database. Only ALC was reviewed retrospectively by retrieving computerized medical records. All patients met the guidelines for APBSCT formulated by the

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National Health Insurance Corporation. All patients gave written informed consent.

General eligibility and exclusion criteria

To be eligible for the study, all patients had to be younger than 65 years of age, have an Eastern Cooperative Oncology Group (ECOG) performance status[9] of 0–2 at the time of transplantation, and a life expectancy $\geqslant 8$ weeks. In addition, there could be no evidence of serious organ dysfunction, including those involving the renal, hepatic, cardiac, pulmonary, central nervous system, and metabolic functions.

Exclusion criteria included the presence of a human immunodeficiency virus or human T-cell lymphoma virus-1 associated malignancy, or an involvement of the central nervous system in NHL. In addition, patients with a history of other malignant diseases in the previous 5 years, except for squamous cell or basal cell carcinoma of skin or stage I uterine cervical carcinoma or cervical carcinoma *in situ*, were excluded from the study.

Disease

All patients had a biopsy-proven diagnosis of T-cell NHL. All enrolled patients had T-cell NHL with a partial response (PR) after four cycles of CHOP (cyclophosphamide, adriamycin, vincristine, prednisolone) chemotherapy, a first complete response (CR) with a high risk of relapse, or chemotherapy-sensitive relapse.

Mobilization and collection of autologous stem cells

SCs were mobilized with a regimen including cyclophosphamide. Alternatively, for patients in whom control of disease was important, SCs were mobilized with ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) supported by lenograstim. Lenograstim (10 μg/kg/day) was infused intravenously until the completion of autologous stem cells (ASCs) collection, and mononuclear cells (MNCs) and $CD34^+$ cells were collected using blood cell separator CS-3000® Plus (Baxtor, USA). At least 5×10^6 $CD34^+$ cells/kg was the recommended dosage among collected MNC.

Conditioning regimens

The primary conditioning regimen was BEAC (carmustine, etoposide, cytarabine, cyclophosphamide), with BEAM (carmustine, etoposide, cytarabine, melphalan) or Vanderbilt (cyclophosphamide, VP-16, vincristine, bleomycin, methotrexate, leucovorin, prednisolone, mesna) regimens used in small numbers of patients. Lenograstim (10 μg/kg/day) was given until hematological engraftment, defined as the first day of an absolute neutrophil count (ANC) $\geqslant 1000$ cells/μl and observed for 2 consecutive days without lenograstim support.

Absolute lymphocyte count and absolute lymphocyte count recovery

White blood cell (WBC) counts were performed using XE-2100™ (SYSMEX Co., Japan), and the percentage of lymphocytes was counted microscopically after Wright staining. ALC was determined by calculating the product of the total WBC count and the percentage of lymphocytes. Complete blood count was checked every day until hematological engraftment, and ALC was measured every day until it reached 500 cells/μl. Thereafter, it was followed until it recovered to its pretreatment value.

We focused on ALC recovery rather than on ALC at some point in time. ALC recovery was determined by the following method. When ALC exceeded 100 cells/μl for at least 3 consecutive days, we considered the patient to have recovered ALC of $\geqslant 100$ cells/μl, and the first of the 3 days was considered the date of ALC recovery to $\geqslant 100$ cells/μl and used to calculate the number of days from the first date of APBSCT to recovery of $\geqslant 100$ cells/μl. Similar methods were utilized to calculate recovery days for ALC $\geqslant 300$, $\geqslant 500$, and $\geqslant 1000$ cells/μl.

Responses and survival

CR was defined as disappearance of all measurable or evaluable disease, signs, symptoms, and biochemical changes related to the tumor for greater than 4 weeks, during which no new lesions appeared. If hepatic or BM involvement had been documented histologically, rebiopsy was required. PR was defined as disappearance of BM involvement by conventional bilateral BM examination without any progression of pre-existing lesions or appearance of new lesions. Alternatively, when compared with pretreatment measurements, PR was defined as a reduction of $>50\%$ in the sum of the products of the longest perpendicular diameters of all measurable lesions lasting for greater than 4 weeks, during which no new lesions appeared, and no existing lesion enlarged $>25\%$.

Response status before and after APBSCT was classified as CR, PR, primary refractory, sensitive relapse, resistant relapse, or first relapse without treatment. Treatment-related mortality was defined as death caused by a treatment procedure or by treatment-related complications within a month after APBSCT. Chemosensitive disease was defined as CR or PR by response status.

The starting point for various time intervals was the starting day of ASCT. The date of the disease progression or relapse was used in calculating progression-free survival (PFS). Time to death, whatever the cause of death, was used to calculate overall survival (OS).

Statistical analysis

For scale variables, data are given as medians and means $\pm$ standard errors of mean (with range in parentheses), while for nominal variables, data are given as number of patients (with percentage in parentheses) if not specified otherwise. All statistical confidence intervals are 95%. To access the OS and PFS, the Kaplan–Meier method was used. Two-tailed log-rank tests were used to compare OS and PFS curves. Prognostic factors tested were age, stage at diagnosis, international prognostic index (IPI), the number of extranodal involvements, the number of prior chemotherapies, chemosensitivity prior to APBSCT, performance status, infused MNC dose, infused dose of $CD34^+$

cells, total dose of supporting lenograstim, recovery days for ALC, recovery days for ANC, recovery days for platelets, and serum lactic dehydrogenase (LDH). Because a cutoff of ALC $\geqslant 1000$ cells/μl had most of the significant differences in OS and PFS, all patients' data were stratified according to the recovery days for ALC $\geqslant 1000$ cells/μl on day $+25$ after APBSCT. The applied ALC recovery days were based on their median values in study groups and were confirmed after testing various days for greater survival differences. To compare the differences between two groups according to ALC recovery days, χ^2 or Fisher's exact test was used for nominal variables and the Mann–Whitney U test was used for scale variables. Continuous covariates were encoded as binary covariates after dichotomization, using the median or known prognostic values as the cutoff. Multivariate prognostic analyses were performed for OS and PFS using Cox models in which all covariates were introduced that were associated with the corresponding outcome at $P<0.1$ by the log-rank test. All P-values were two sided, with $P<0.05$ indicating statistical significance.

Results

Patient characteristics

A total of 39 patients with T-cell NHL were enrolled in the study. Six of the 39 patients were later deemed ineligible because of early death, defined as mortality within 1 month of APBSCT without full hematological recovery, and independent of the cause of death. Of the 33 patients analyzed, none was lost to follow-up. Neither CD34-positive selection nor purging was applied. The median age was 35 with a mean value of 35.61 ± 2.10 (range, 18–61 years). There were more males (72.7%) than females (27.3%). Most patients (78.8%) received BEAC. Most common histological subtypes were peripheral T-cell lymphoma, not otherwise characterized, and precursor T-cell lymphoblastic lymphoma/acute lymphoblastic leukemia. The basic clinical characteristics are summarized in Table 1, and their detailed histological subtypes are shown in Table 2.

Two of the 33 (6%) patients enrolled in our study failed to reach the level of ALC $\geqslant 1000$ cells/μl, while over 90% attained this level within 40 days. When the groups were stratified according to ALC of <1000 or $\geqslant 1000$ cells/μl by day $+25$ after APBSCT, there were no differences in prognostic factors including gender, LDH level, IPI, extranodal sites involvement, numbers of pretransplantation chemotherapy cycles, age at APBSCT, disease status at APBSCT, performance status, infused MNC dose, infused CD34+ cell dose, total lenograstim dose, platelets $\geqslant 20 \times 10^3/\mu$l on day $+15$, and ANC $\geqslant 500$ cells/μl on day $+12$ (Table 3).

Survival

Of the 33 patients, 20 (60.6%). died by March 2003, eight (24.2%) from disease progression, eight (24.2%) from various infections, and four (12.1%) from causes other than NHL. Median follow-up was 46.5 months, with a mean value of 55.4 ± 5.6 months (range, 9.9–129.4 months). Two of the 33 patients (6.1%) did not reach ALC $\geqslant 1000$ cells/μl before death.

Table 1 Basic characteristics of patients

Characteristic	*No. of patients (%)*		
Gender			
Male	24 (72.7)		
Female	9 (27.3)		
Stage III or IV at diagnosis	22 (66.7)		
IPI at diagnosis high–intermediate and high	13 (39.4)		
CR or PR disease status at APBSCT	26 (78.8)		
Performance status at diagnosis ECOG 0–1	25 (75.8)		
Conditioning regimen			
BEAC	26 (78.8)		
Vanderbilt	5 (15.2)		
BEAM	2 (6.1)		
	Median	*Mean* $\pm$ *s.e.*	*Range*
Age (years)	35	35.61 ± 2.10	18–61
No. of pretransplantation chemotherapy cycles	6	6.48 ± 0.786	2–25
Number of extranodal involvements	1	1.06 ± 0.043	0–2
Serum LDH at diagnosis (IU/l)	499.5	1110 ± 218.81	191–5365
Infused MNC dose at ASCT ($\times 10^8$/kg)	4.1	4.75 ± 0.52	1.53–15.86
Infused CD34+ cell dose ($\times 10^6$/kg)	8.29	11.64 ± 1.70	2.96–36.68
Total supporting lenograstim dose (μg)	3500	4417.19 ± 539.95	1200–17200
Days to recovery of ANC $\geqslant 500$ cells/μl	12	15.48 ± 1.48	8–49
Days to recovery of ALC $\geqslant 500$ cells/μl	19	23.41 ± 2.90	13–106
Days to recovery of ALC $\geqslant 1000$ cells/μl	26	30.61 ± 3.39	12–106
Days to recovery of platelets $\geqslant 20 \times 10^3/\mu$l	15	16.52 ± 1.17	5–36

IPI = international prognostic index; NHL = non-Hodgkin's lymphoma; CR = complete remission; PR = partial remission; LDH = lactic dehydrogenase; ANC = absolute neutrophil count; ALC = absolute lymphocyte count; BEAC (carmustine, etoposide, cytarabine, cyclophosphamide); BEAM (carmustine, etoposide, cytarabine, melphalan); Vanderbilt (cyclophosphamide, VP-16, vincristine, bleomycin, methotrexate, leucovorin, prednisolone, mesna).

Table 2 Detailed histological subtypes relative to recovery of ALC $\geqslant 1000$ cells/μl by day $+25$

Histological subtype	*$\leqslant 25$ days ($n=13$)*	*>25 days ($n=20$)*
	No. (%)	*No. (%)*
PTCL, not otherwise characterized	4 (12.1)	9 (27.3)
Precursor T-LBL/ALL	6 (18.2)	6 (18.2)
Extranodal NK/T-cell lymphoma, nasal type	1 (3)	2 (6.1)
Anaplastic large-cell lymphoma, T/null cell, primary cutaneous type	1 (3)	2 (6.1)
Anaplastic large-cell lymphoma, T/null cell, primary systemic type	1 (3)	0 (0)
Angioimmunoblastic T-cell lymphoma	0 (0)	1 (3)

PTCL = peripheral T-cell lymphoma; NK = natural killer; LBL = lymphoblastic lymphoma; ALL = acute lymphoblastic leukemia.

Table 3 Comparison of groups relative to recovery of ALC $\geqslant 1000$ cells/μl by day $+25$

Characteristic	*$\leqslant 25$ days ($n=13$)*	*>25 days ($n=20$)*	*P-value*
Gender (%)			1.0
Male	30.3	42.4	
Female	9.1	18.2	
Prognostic factors at diagnosis (%)			
LDH level (IU/l, >2-fold above UNL)	21.2	33.3	0.948
IPI ($\geqslant$high–intermediate)	12.1	27.3	0.485
Extranodal sites ($\geqslant 2$)	6.1	9.1	1.0
No. of pretransplantation chemotherapy cycles (median)	5	6	0.298
Prognostic factors at APBSCT (%)			
Age (>45 years)	15.2	9.1	0.213
Disease status (CR or PR)	36.4	42.4	0.202
Performance status ($\geqslant 2$)	6.1	18.2	0.431
Prognostic factors during APBSCT (median)			
Infused MNC dose at ASCT ($\times 10^8$/kg)	4.88	3.72	0.173
Infused CD34+ cell dose ($\times 10^6$/kg)	9.18	6.78	0.167
Total lenograstim dose (μg)	3250	3500	0.326
Prognostic factors after APBSCT (%)			
Platelets $\geqslant 20\times 10^3/\mu$l on day $+15$	24.2	33.3	0.710
ANC $\geqslant 500$ cells/μl on day $+12$	27.3	30.3	0.310

Improved OS and PFS were observed in the patients who required less than 25 days from ABSCT to recovery of ALC $\geqslant 1000$ cells/μl (Figure 1) (not reached *vs* 7 months, $P=0.0119$; not reached *vs* 4.5 months, $P=0.0117$, respectively). In contrast, for patients who recovered ALC $\geqslant 500$ cells/μl at day $+19$, statistical significance was reached only for PFS (OS, $P=0.0853$; PFS, $P=0.0456$).

When various days (range, 6–23 days) were tested for ALC $\geqslant 100$, $\geqslant 300$, and $\geqslant 500$ cells/μl, all revealed no correlations with OS and PFS. Only ALC $\geqslant 1000$ cells/μl showed a correlation with OS and PFS.

Univariate analysis

Many prognostic factors were associated with OS or PFS, including chemosensitive response prior to APBSCT (CR or PR disease status *vs* relapse/refractory at APBSCT), recovery of ALC $\geqslant 1000$ cells/μl (>25 *vs* $\leqslant 25$ days), recovery of ALC $\geqslant 500$ cells/μl (>19 *vs* $\leqslant 19$ days), performance at diagnosis (ECOG >1 *vs* $\leqslant 1$), age(>45 *vs* $\leqslant 45$ years), IPI at diagnosis ($\geqslant$high–intermediate *vs* $<$high–intermediate), and numbers of extranodal involvements (>1 *vs* $\leqslant 1$). Stage at diagnosis ($>$II *vs* $\leqslant$II), numbers of pretransplantation chemotherapy cycles (>6 *vs* $\leqslant 6$ cycles), infused MNC dose at ASCT (>4.4 *vs* $\leqslant 4.4\times 10^8$/kg), total lenograstim dose (>3500 *vs* $\leqslant 3500$ μg), recovery of ANC $\geqslant 500$ cells/μl (>12 *vs* $\leqslant 12$ days), and recovery of platelets $\geqslant 20\times 10^3$ cells/μl (>15 *vs* $\leqslant 15$ days) were not predictive of OS and PFS. All data are given in Table 4.

Multivariate analysis

Multivariate analysis was performed based on factors having a *P*-value of <0.1 by univariate analysis. Chemosensitive response prior to APBSCT was a positive predictor for better OS (RR = 7.167, $P=0.005$) and PFS (RR = 30.243; $P\leqslant 0.001$). ALC was predictive for better OS (RR = 6.005, $P=0.011$) and PFS (RR = 6.810, $P=0.013$) only in ALC $\geqslant 1000$ cells/μl at day $+25$. Recovery of ALC $\geqslant 500$ cells/μl at day $+19$ failed to show significance in multivariate analysis, although it was a predictor of better PFS in univariate analysis. Performance at diagnosis, age, IPI at diagnosis, and numbers of extranodal involvements were not significant in multivariate analysis. Table 5 summarizes the significant predictors for OS and PFS identified in the multivariate analysis.

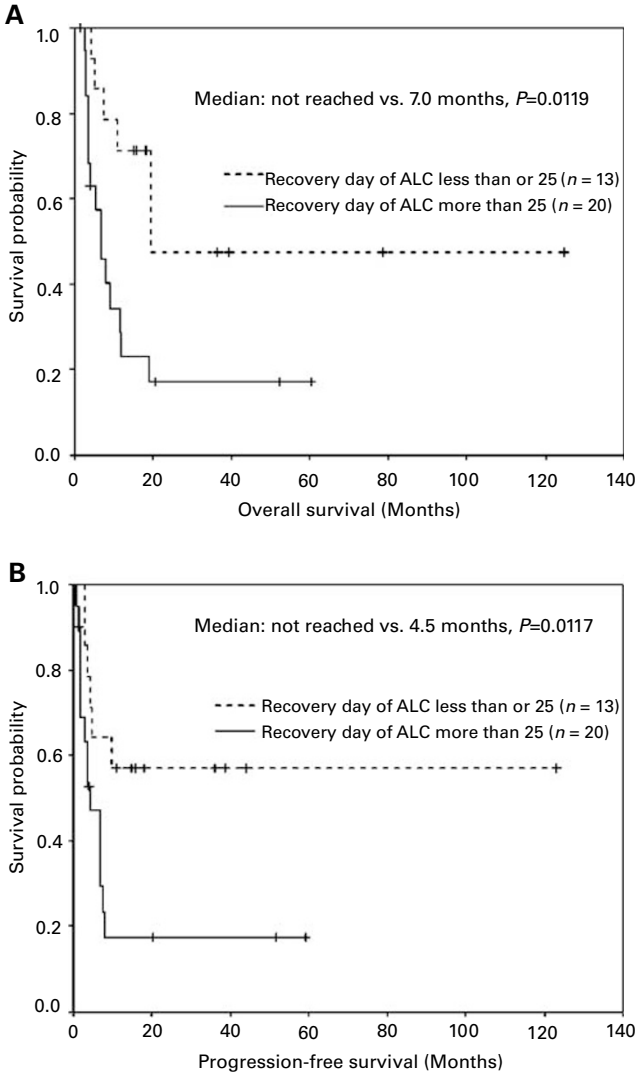

Figure 1 Survival probability of 33 patients with T-cell NHL receiving APBSCT relative to days required to recover ALC $\geqslant$1000 cells/μl (Kaplan–Meier curves): (**a**) OS curve; (**b**) PFS curve.

Discussion

Previously reported ASCT data in patients with MM, NHL, Hodgkin's lymphoma, and metastatic breast cancer showed evidence of association between survival and early lymphocyte recovery.[6,7,10] Our results are distinguished from previous reports in that ALC recovery of 500 cells/μl could not be correlated with survival. In contrast, we found that ALC recovery of 1000 cells/μl within 25 days of APBSCT was associated with better OS and PFS in T-cell NHL. Among the differences between our data and those reported previously are that we utilized PB as a source of SCs, whereas previous studies utilized both PB and BM. In addition, we excluded APBSCT patients with early mortality, whereas other studies did not. By including these patients, the role of early lymphocyte recovery in long-term survival could not be clarified easily. In contrast, by excluding these patients, we sought to evaluate the prognostic significance of lymphocyte recovery on long-term survival.

Our findings raise several important questions. By what mechanism does ALC recovery contribute to longer survival? Why is improvement in survival not related to ALC recovery of 500 cells/μl but is related to recovery of 1000 cells/μl? Does APBSCT differ from ASCT using BM? To answer these questions, we have to know more about immune reconstitution after ASCT, because immune reconstitution after HSCT is a matter of concern, both with respect to immunological restoration and its potential antitumor effects.

From what we know, the early post transplant period is characterized by rapid recovery of naïve CD8+ cells, delayed reconstitution of $CD4^+/CD45RA^+$ T cells, and a compensatory increase in the number of $CD28^-$ T cells, under the influence of thymic output after autologous PBSC.[11–15] Natural killer (NK) cells usually reach a normal value within a month, and dendritic cells (DCs) reach a preconditioning level on day +20 and nearly normal levels after day +180. In contrast, B cells show delayed recovery, even after 3 months.[12,16,17] Our finding, that ALC recovery

Table 4 Univariate analysis in relation to OS and PFS

Prognostic factor	*OS (P-value)*	*PFS (P-value)*
Age >45 *vs* $\leqslant$ 45 years	0.0292	0.0267
LDH level (IU/l) >2-fold above UNL *vs* $\leqslant$2-fold	0.1186	0.0879
IPI at diagnosis $\geqslant$high–intermediate *vs* <high–intermediate	0.0543	0.0267
Stage at diagnosis (>II *vs* $\leqslant$II)	0.7841	0.4844
Performance at diagnosis (ECOG) >1 *vs* $\leqslant$1	0.2452	0.0818
No. of extranodal involvements >1 *vs* $\leqslant$1	0.3005	0.0774
No. of pretransplantation chemotherapy cycles >6 *vs* $\leqslant$6	0.1852	0.4763
CR or PR disease status *vs* relapse/refractory at APBSCT	0.0003	<0.0001
Infused MNC dose at ASCT ($\times 10^8$/kg) >4.4 *vs* $\leqslant$4.4	0.2621	0.2655
Infused CD34+ cell dose ($\times 10^6$/kg) >7.8 *vs* $\leqslant$7.8	0.2995	0.1789
Total lenograstim dose >3500 *vs* $\leqslant$ 3500 μg	0.7977	0.8712
Recovery of ALC $\geqslant$500 cells/μl >15 *vs* $\leqslant$15 days	0.2660	0.2039
Recovery of ALC $\geqslant$500 cells/μl >19 *vs* $\leqslant$19 days	0.0853	0.0456
Recovery of ALC $\geqslant$1000 cells/μl >25 *vs* $\leqslant$25 days	0.0119	0.0117
Recovery of ANC $\geqslant$500 cells/μl >12 *vs* $\leqslant$12 days	0.5119	0.3839
Recovery of platelets $\geqslant$20 $\times$ 103 cells/μl >15 *vs* $\leqslant$15 days	0.4374	0.3100

Table 5 Multivariate analysis in relation to OS and PFS

Prognostic factors	*OS*			*PFS*		
	P-value	*RR*	*95% CI*	*P-value*	*RR*	*95% CI*
Recovery of ALC $\geqslant$1000 cells/μl $>$25 *vs* $\leqslant$ 25 days	0.011	6.005	1.515–23.799	0.013	6.810	1.493–31.056
Recovery of ALC $\geqslant$500 cells/μl $>$19 *vs* $\leqslant$ 19 days	0.422	0.602	0.175–2.074	0.194	0.368	0.081–1.664
CR or PR disease status *vs* relapse/refractory at APBSCT	0.005	7.167	1.815–28.307	$<$0.001	30.243	4.527–202.035
IPI at diagnosis $\geqslant$high–intermediate *vs* $<$high–intermediate	0.754	0.723	0.095–5.503	0.563	1.834	0.235–14.293
No. of extranodal involvements $>$1 *vs* $\leqslant$1	0.766	0.765	0.131–4.477	0.115	3.549	0.736–17.104
Age $>$45 *vs* $\leqslant$45 years	0.290	0.411	0.079–2.133	0.159	0.295	0.054–1.616
Performance status at diagnosis $>$1 *vs* $\leqslant$1	0.446	0.575	0.139–2.383	0.834	0.845	0.176–4.072
LDH at diagnosis $>$2-fold of UNL *vs* $\leqslant$2-fold of UNL	0.232	3.198	0.475–21.507	0.889	0.869	0.121–6.255

RR = Relative risk; CI = Confidence interval; UNL = upper normal limit.

around day +25 is predictive for better PFS, suggests that T cells, NK cells or DCs may manifest immune-mediated antitumor activities. When considering all the dynamics of immune reconstitution, it may be that mainly T cells and DCs can elicit protective antitumor effects against minimal residual disease (MRD) around 25 days after APBSCT, that is, when ALC reached 1000 cells/μl. In addition, NK cells may also play a role in the antitumor effects. In an early period after APBSCT, the reconstituted cells do not have the capacity to produce a sufficient amount of interferon gamma and B-cell function does not yet return to baseline.[18] Therefore, the role of humoral immunity against MRD may be minor.

The hematological dynamics of PB resemble those of BM as a source of ASCT. After peripheral blood stem cell transplantation (PBSCT), the absolute numbers of total circulating lymphocytes and lymphocyte subpopulations are not significantly different from those after BMT or after high-dose regimens.[19,20] Although the hematological recoveries after PBSCT are similar to those after bone marrow stem cell transplantation (BMSCT), there are differences between the two in some immunological aspects.[7,21,22] G-CSF-induced activated T cells, which are collected during SC collection and infused during SC support, can play a role during APBSCT, but not during ABMSCT.[23]

Only 2/33 patients enrolled in our study failed to reach the level of ALC $\geqslant$1000 cells/μl, while over 90% attained this level within 40 days. Moreover, we found that ALC $\geqslant$500 cells/μl on day +15 failed to have prognostic significance, in that it did not predict survival of patients without early mortality within a month after APBSCT. Our results suggest that ALC $\geqslant$1000 cells/μl on day +25 is a better predictor for long-term survival than ALC $\geqslant$500 cells/μl on day +15 in T-cell NHL.

The incidence and proportion of lymphomas in Western countries differ from those in oriental countries. For example, among lymphoid malignancies, the incidence of Hodgkin's is 33% in the United States, but less than 6.8% in Korea.[24,25] Among patients with NHL, T-cell NHL has a relatively low incidence compared with B-cell NHL. T-cell NHL comprises about 35.2% of the NHL cases in Korea, which is much higher than the 12% worldwide incidence, with most of the latter cases coming from Hong Kong.[26,27]

In conclusion, lymphocyte recovery resulting from immune engraftment (APBSCT) is strongly associated with long-term survival and PFS in T-cell NHL. To our knowledge, this is the first such report dealing with the prognostic significance of ALC recovery in the setting of APBSCT for T-cell NHL. Further study is warranted to define recovery relative to immunologic subsets contributing to the suppression of MRD after APBSCT and to compare the immunologic responses in patients with T-cell NHL with those in patients with B- cell NHL.

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