Original Article

Outcomes of Adults with Acute Lymphoblastic Leukemia After Autologous Hematopoietic Stem Cell Transplantation and the Significance of Pretransplantation Minimal Residual Disease: Analysis from a Single Center of China

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Abstract

Background: The postremission therapies for adult patients generally contain consolidation chemotherapy, allogeneic hematopoietic stem cell transplantation and autologous hematopoietic stem cell transplantation (auto-HSCT). Because of the various results from different centers, the optimal therapy for adult acute lymphoblastic leukemia (ALL) patients is still uncertain. This study aimed to better understand predictive factors and role of auto-HSCT in the postremission therapy for adult ALL patients.

Methods: The outcomes of 135 adult patients with ALL, who received the first auto-HSCT in Hematopoietic Stem Cell Transplantation Center of Blood Diseases Hospital, Chinese Academy of Medical Sciences from January 1, 1994 to February 28, 2014, were retrospectively analyzed. Survival curves were estimated using the Kaplan-Meier method and simultaneous effects of multiple covariates were estimated with the Cox model.

Results: Overall survival (OS) and disease-free survival (DFS) at 5 years for the whole cohort were 59.1 ± 4.5% and 59.0 ± 4.4%, respectively. The cumulative nonrelapse mortality and relapse rate at 5 years were 4.5 ± 0.03% and 36.6 ± 0.19%. For both OS and DFS, acute T-cell lymphoblastic leukemia, high lactate dehydrogenase (LDH) at diagnosis, blast cell proportion ≥5% on the 15th day of induction therapy, and extramedullary infiltration before HSCT were the poor prognosis factors. In addition, age ≥35 years predicted poor DFS. Only T-ALL and high LDH were the independent undesirable factors associated with OS and DFS in Cox regression model. For 44 patients who had results of pretransplantation minimal residual disease (MRD), positive MRD (MRD ≥0.01%) indicated poor OS ($P = 0.044$) and DFS ($P = 0.008$). Furthermore, for the standard risk group, the patients with negative MRD (MRD <0.01%) had better results (OS at 18 months was 90.0 ± 9.5%, while for the patients with positive MRD OS was 50.0 ± 35.4%, $P = 0.003$; DFS at 18 months was 90.0 ± 9.5%, while for the positive MRD group DFS was 0%, $P < 0.001$).

Conclusions: This study confirmed that auto-HSCT combined with posttransplantation maintenance chemotherapy could be an option for adult ALL patients and pretransplantation MRD may play a significant role in the direction of therapy for adult ALL patients.

Key words: Acute Lymphoblastic Leukemia; Adult; Autologous Hematopoietic Stem Cell Transplantation; Minimal Residual Disease; Prognostic Factors

Introduction

The postremission therapies for adult patients generally contain consolidation chemotherapy, allogeneic hematopoietic stem cell transplantation (allo-HSCT), and autologous hematopoietic stem cell transplantation (auto-HSCT). The chemotherapy alone may not provide a long duration of remission,[1] while lack of the suitable donor and the nonignorable mortality of severe graft-versus-host disease are the significant obstacles for the allo-HSCT. Consequently, auto-HSCT may be a potential choice. Although some analyses about auto-HSCT did not find out the obvious advantages compared with chemotherapy alone.[2] Because of the various results from different centers,[3-5] the optimal therapy for adult acute lymphoblastic leukemia (ALL) patients is still uncertain. However, the report from our hospital indicated that compared with chemotherapy group, the auto-HSCT group had lower cumulative relapse rate (32.35% vs. 70%),

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and better 5-year overall survival (OS) (55.9 ± 8.5% vs. 24.9 ± 7.4%) and leukemia-free survival (55.9 ± 8.5% vs. 23.4 ± 7.3%).[6] Meanwhile, outcomes of a research from Anhui Medical University Provincial Hospital[7] demonstrated that 3-year OS and disease-free survival (DFS) of chemotherapy for adult ALL patients were lower (both OS and DFS <50%) than our results of auto-HSCT. Similarly, 3-year DFS rate of the French protocol leucémie aiguës lymphoblastique de l'adulte 87 trial was 41%,[2] which was also lower than our results. Taken together, because of the undesired results of chemotherapy from Chinese or abroad, most patients were suggested the auto-HSCT when they did not have a suitable donor, even for the standard risk (SR) patients. This retrospective study was performed to explore the predictive factors and the role of auto-HSCT in the postremission therapy for ALL patients.

Methods

Data collection and patients

The eligible candidates must comply with the criteria as follows: (1) Age >15 years old; (2) patients underwent first auto-HSCT at Hematopoietic Stem Cell Transplantation Center of Blood Diseases Hospital, Chinese Academy of Medical Sciences between January 1, 1994 and February 28, 2014; (3) follow-up data were available. Collected data included characteristics of patients and diseases, therapy before HSCT, details of stem cells, minimal residual disease (MRD), conditioning regimens, duration of posttransplantation remission and outcome variables, including OS, DFS, nonrelapse mortality (NRM) and relapse.

Risk stratification

According to Helbig *et al*.,[8] high risk (HR) was defined as having any of the following poor-risk factors: (1) Age ≥35 years, (2) high white blood cell (WBC) count (>30 × 10^9/L for B-cell lineage and >100 × 10^9/L for T-cell lineage), (3) pro-B, early-T and mature T immunophenotype, (4) second or greater complete remission (CR), (5) the presence of adverse cytogenetics: Philadelphia chromosome positive (Ph-positive), that is, t(9;22) and/or *BCR-ABL* transcripts; 11q23 abnormality and/or *MLL-AF4* transcripts; t(1;19) and/or *E2A-PBX1* transcripts; complex karyotype and hypodiploidity. Patients without any factors mentioned above were considered as SR group. As a result, 46 patients were classified into SR group and 89 patients were grouped into HR group.

Treatment

Induction and early consolidation/intensification chemotherapy. All patients newly diagnosed in our center were given a standard 4 or 5 drugs induction regimen VDCP ± L (vincristine [VCR] 1.4 mg·m^{-2}·d^{-1}, maximum 2 mg/d, days 1, 8, 15, and 22; daunorubicin 45 mg·m^{-2}·d^{-1}, days 1–3 and 15–17; cyclophosphamide (CY) 750 mg·m^{-2}·d^{-1}, days 1 and 8; and prednisone (Pred) 1 mg·kg^{-1}·d^{-1}, days 1–28; with or without L-asparaginase 6000 U·m^{-2}·d^{-1}, days 5, 8, 11, 15, 18, and 22) for 28 days. Patients who reached CR were treated with consolidation chemotherapy, which contains several regimens such as high-dose methotrexate (MTX) (2 g·m^{-2}·d^{-1}, day 1), CAM (CY 750 mg·m^{-2}·d^{-1}, days 1 and 15; arabinoside cytarabine (Ara-C) 200 mg·m^{-2}·d^{-1}, days 1–3 and 8–10; 6-mercaptopurine 60 mg·m^{-2}·d^{-1}, generally 100 mg/d, p.o., days 1–7), dexamethasone (DOAME) 0.15 mg·kg^{-1}·d^{-1}, days 1–5; VCR 1.4 mg·m^{-2}·d^{-1}, maximum 2 mg/d, day 1; Ara-C 2 g·m^{-2}·d^{-1}, days 1–3; mitoxantrone 8 mg·m^{-2}·d^{-1}, days 2 and 3; etoposide 0.1 g/d, days 3–5), etc. Patients who received induction chemotherapy in other hospitals were firstly assessed in the treatment processes and disease status, and then they were given re-induction or systematic intensive chemotherapy. Ph-positive ALL patients who were diagnosed after 2006 (13/15) received tyrosine kinase inhibitors (TKIs) as long as the Philadelphia chromosome was demonstrated. The other two patients did not take TKIs because the TKIs had not been widely employed at the early time.

Conditioning regimen

All patients received a myeloablative conditioning regimen before HSCT. Most of them (131/135) were treated with single traumatic brain injury (TBI) (7–10 Gy) followed by CY (40 mg·kg^{-1}·d^{-1} for 2 days) or high-dose melphalan (140 mg·m^{-2}·d^{-1} for 1 day), additional high-dose Ara-C (2 g·m^{-2}·d^{-1} for 3 days), and fludarabine (30 mg·m^{-2}·d^{-1} for 4 days) or high-dose etoposide-16 (1000 mg·m^{-2}·d^{-1} for 1 day). Two patients received regimen as above just except TBI, and the other two without TBI were given BU + Mel (BU 3.2 mg·kg^{-1}·d^{-1} for 4 days; Mel 180 mg·m^{-2}·d^{-1} for 1 day).

Stem cell source and autografting

Until 2000, the stem cells were gained from bone marrow (BM) before auto-HSCT during the CR duration. After 2000, most stem cell harvest was performed from peripheral blood after chemotherapy-induced mobilization combined with recombinant G-CSF. DOAME (as mentioned above) was the most used regimen in mobilization (81/106). Others patients were mobilized with high-dose Ara-C-based regimen or high-dose MTX. Patients who failed first mobilization ($CD34^+$ cells <1 × 10^6/kg within 2 collection days) were remobilized after another chemotherapy or collected from BM as a complement. Finally, 29 patients received BM stem cell transplantation, 100 patients were performed with peripheral blood stem cell transplantation, and the other 6 patients' stem cells came from BM and peripheral blood. Median mononuclear cells and $CD34^+$ cells infused were 4.10 × 10^8/kg (range 1.00–12.5 × 10^8/kg) and 2.77 × 10^6/kg (range 0.65–28.13 × 10^6/kg), respectively.

Maintenance therapy

When WBC reached 3 × 10^9/L and platelets reached 50 × 10^9/L after auto-HSCT, the patients began to be given the maintenance therapy which may be continued for 1–1.5 years. The therapy generally based on VP regimen (VCR 1.4 mg/m^2, maximum 2 mg, i.v., days 1 and 8; Pred 30–40 mg/d, p.o., days 1–14), and multiple myeloma regimen (6-mercaptopurine 60 mg·m^{-2}·d^{-1}, generally 100 mg/d, p.o., days 1–14; MTX 20 mg·m^{-2}·d^{-1}, generally

30 mg/d, p.o., days 1 and 8) was administered alternatively. In addition, for Ph-positive ALL patients, TKI was also in the list of alternative regimens.

Definitions and statistical analysis

For patients without an event, observation was censored at the cutoff date of May 31, 2014. OS was defined as the duration from auto-HSCT to death of any cause or cutoff date. DFS was defined as survival in CR after HSCT. For NRM, death was occurred because of any cause without previous relapse. Cumulative incidences of relapse were determined from the date of HSCT to the date of relapse or last follow-up.

Survival curves were estimated using the Kaplan-Meier method and differences were compared using the log-rank test. Simultaneous effects of multiple covariates were estimated with the Cox model for DFS, OS and relapse rate, and tested by the likelihood-ratio test. The cumulative risks of relapse and NRM over time were calculated as competing risks. The data of normal distribution were described with the forms of mean ± standard deviation (SD), and the median values were used to describe the data with no normal distribution. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and R (R Development Core Team, Vienna, Austria) software packages.

Results

Patients profile

A total of 167 patients with ALL underwent the first auto-HSCT at our center between January 1, 1994 and February 28, 2014. Ultimately, patients whose age <15 years old, complications contained other malignancy, or follow-up data unavailable were excluded, leaving a final study population of 135 patients. Table 1 showed the pretreatment characteristics of the study group. Among these, because of unavailable flow cytometry before 1998, 18 patients did not have the immunophenotyping results.

Table 1: Clinical and biological characteristics of study patients (n = 135)

Characteristics	Values
Male/female, *n*	93/42
Age, years, median (range)	21 (15–54)
WBC, $\times 10^9$/L, median (range)	8.28 (0.57–387.20)
>30×10^9/L for B-cell lineage, >100×10^9/L for T-cell lineage, *n* (%)	39 (28.89)
Immunophenotype, *n* (%)	
B lineage (Mye$^+$)	100 (41)
Pro-B (Mye$^+$)	15 (7)
Common-B (Mye$^+$)	74 (31)
Pre-B (Mye$^+$)	11 (3)
T lineage (Mye$^+$)	17 (3)
ALL without clear immunophenotype, *n*	18
Karyotype and molecular biology, *n*	
Normal	74
t(9;22)/*BCR-ABL*	15
t(4;11)/*MLL-AF4*	3
t(1;19)/*E2A-PBX1*	3
Complex karyotype	11
Hypodiploidity	3
Others	26
Time to achieve CR >4 weeks, *n* (%)	12 (8.89)
Disease status at HSCT, *n* (%)	
CR1	122 (90.40)
CR2 or greater	13 (9.6)

WBC: White blood cell; Mye$^+$: Positive myeloid markers; ALL: Acute lymphoblastic leukemia; CR: Complete remission; HSCT: Hematopoietic stem cell transplantation; CR1: The first complete remission; CR2: The second complete remission.

Hematopoiesis reconstruction

The median time to absolute neutrophil count ≥0.5 × 10^9/L for 3 continuous days and platelet ≥20 × 10^9/L for 7 continuous days without platelet transfusions were 12 days (range 8–44 days) and 16 days (range 6–187 days), respectively. In addition, 6 patients who died of infection and/or hemorrhage in the early stage after HSCT (day +11 to +42) never reconstructed with platelets, and 4 of them did not reached myeloid reconstruction neither before death.

Overall survival, disease-free survival, nonrelapse mortality, and relapse

By the end of May 31, 2014, there were 53 patients died (6 for NRM, and 47 for leukemia relapse). With a median follow-up in all patients of 31.6 months (range 0.4–220.0 months), OS was 76.3 ± 3.7% at 1 year, 61.1 ± 4.4% at 3 years, and 59.1 ± 4.5% at 5 years. DFS ratios at 1, 3, and 5 years were 67.5 ± 2.5%, 59.9 ± 4.3%, and 59.0 ± 4.4%, respectively [Figure 1].

Among the 6 patients (4.4%) of NRM, 3 died from severe pneumonia, 1 patient occurred pulmonary hemoptysis, 1 suffered from liver abscess, and 1 died of lethal coagulopathy. The cumulative incidence of NRM at 5 years was 4.5 ± 0.03%. By the end of follow-up, a total of 49 patients relapsed. Among them, 2 patients relapsed in both of BM and central nervous system, and the others had BM relapsed. The median time from auto-HSCT to relapsed was 149 days (range 27–2134 days), and the cumulative incidence of relapse at 1, 3, and 5 years were 28.0 ± 0.15%, 35.6 ± 0.18%, and 36.6 ± 0.19%, respectively [Figure 2].

Stratified by risk group, survival analysis showed that SR had better OS ($P = 0.002$) and DFS ($P = 0.001$) compared to HR group [Figure 3].

Prognostic factor

Gender, age (<35 years vs. ≥35 years), initial WBC count, blast cells ratio in BM at diagnosis and the 15th day of the first induction therapy, lactate dehydrogenase (LDH) at diagnosis (high vs. normal), T-ALL (among the cases with clear immunophenotype), extramedullary involvement before HSCT, myeloid antigen expression (among the cases with clear immunophenotype), cytogenetic

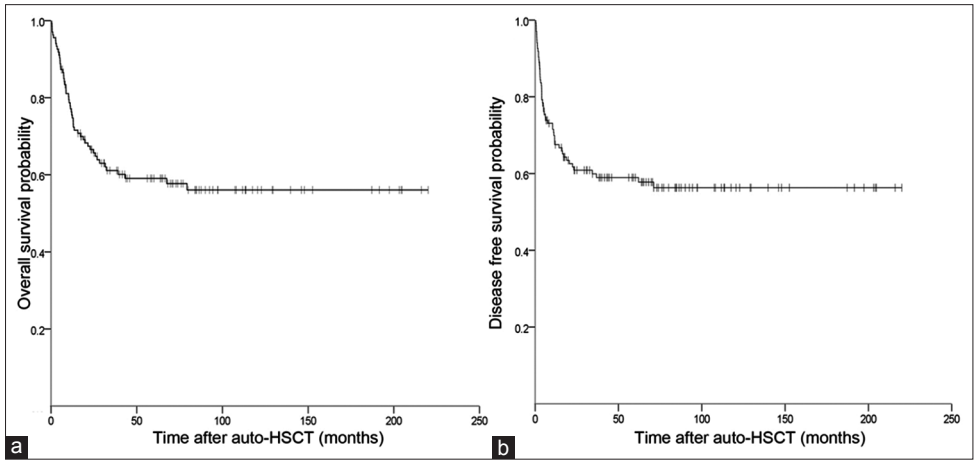

Figure 1: Survival curves after autologous hematopoietic stem cell transplantation. Overall survival (a) and disease-free survival (b) for all patients.

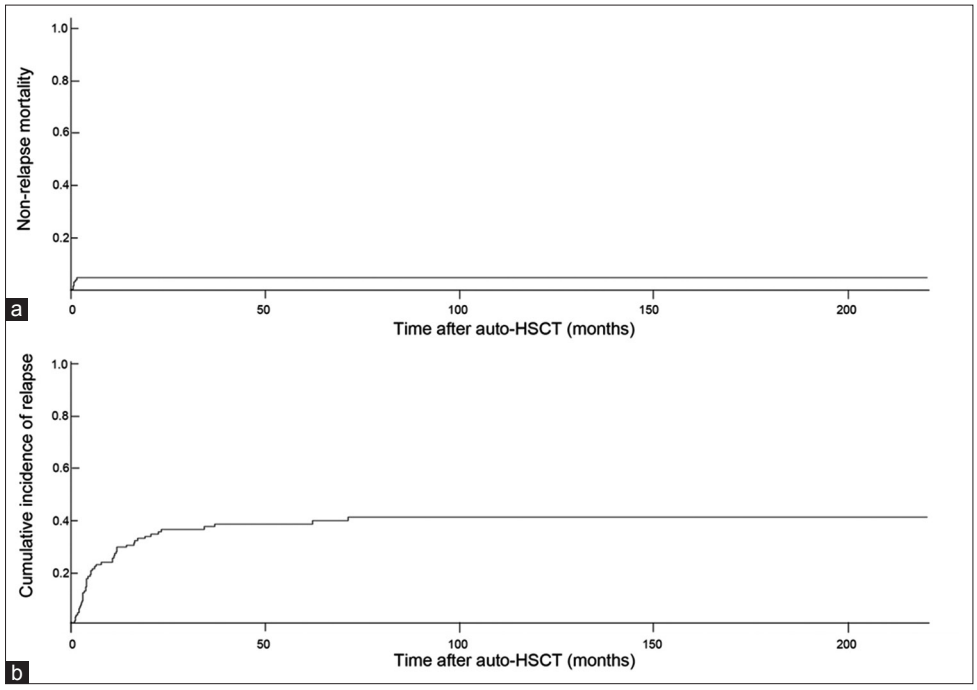

Figure 2: Relapse and mortality not associated with relapse after autologous hematopoietic stem cell transplantation. (a) Nonrelapse mortality of all patients; (b) Cumulative relapse rate of all patients.

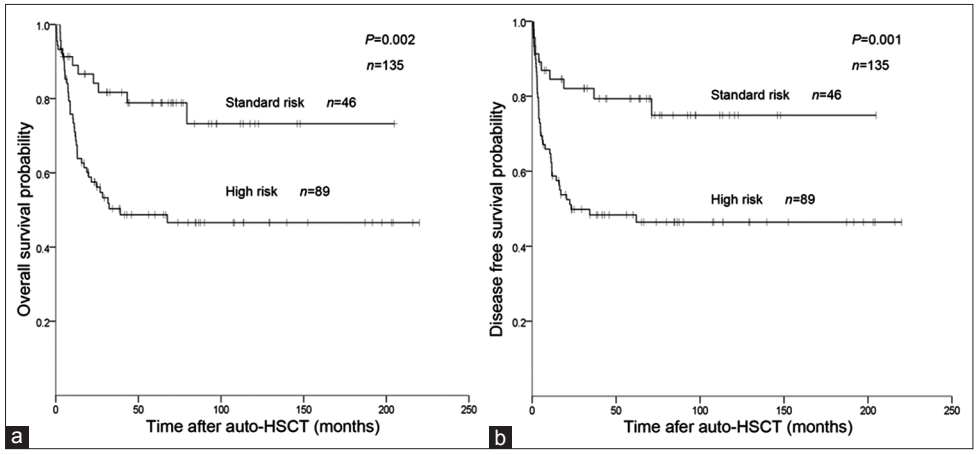

Figure 3: Survival curves of different risk stratification. (a) Overall survival for standard risk (SR) and high risk (HR) groups; (b) Disease free survival for SR and HR groups.

abnormalities (normal vs. abnormal at diagnosis and before transplantation), time to achieve CR1 (≤28 days vs. >28 days), CR to HSCT interval (≥6 months vs. <6 months), and timing of transplantation (at CR1 vs. CR2/greater) were brought into univariate analysis. For both OS and DFS, T-ALL, high LDH at diagnosis, blast cell proportion ≥5% on the 15th day of induction therapy and extramedullary infiltration before HSCT were the poor prognosis factors. In addition, age ≥35 years predicted poor DFS. However, only T-ALL and high LDH were the independent undesirable factors associated with OS and DFS in Cox regression model [Table 2].

Significance of minimal residual disease

After 2010, the MRD detection by flow cytometry was widely applied gradually, and 44 patients had pretransplantation MRD test within 1 month prior to HSCT. Because of the limited number of cases, the MRD results were not putted into the Cox regression analysis. Kaplan-Meier method was used in the assessment of MRD, and the results showed that patients with positive pretransplantation MRD (MRD ≥0.01%) had a poor OS ($P = 0.044$) and DFS ($P = 0.008$). Five out of 6 patients with positive MRD experienced relapse, versus 10 out of 38 patients with negative MRD (MRD <0.01%). The DFS at 5 years were 0% and 68.6 ± 8.5%, respectively. Furthermore, for the SR group, the patients with MRD negative (MRD <0.01%) had a better results (OS at 18 months were 90.0 ± 9.5% vs. 50.0 ± 35.4%, $P = 0.003$; DFS at 18 months were 90.0 ± 9.5% vs. 0%, $P < 0.001$) compared with the positive group. Three of 4 patients with a positive result in HR group relapsed, while 9 of 25 patients whose MRD was negative occurred leukemia after transplantation [Figure 4].

Thirty-three patients had the MRD results of autograft. Among the thirty patients with negative autograft MRD, 9 patients relapsed; one of the 2 patients with MRD = 0.01% suffered from relapse; and 1 patient whose MRD >0.01% relapsed within 120 days after auto-HSCT. Although the cases were limited, there was a definite trend that patients whose graft MRD was negative had better outcomes.

Discussion

By now, for the adult ALL patients who achieved CR1 after induction chemotherapy, sibling allo-HSCT was the preferred approach when the human leukocyte antigen (HLA)-identical sibling was available, then, the HLA-matched unrelated

Table 2: Prognostic factors in univariate and multivariate analysis

Outcomes	Factors	Univariate	Multivariate		
		P	*P*	*RR*	95% *CI*
OS	T-ALL	0.000	0.015	2.703	1.213–6.022
	LDH at diagnosis	0.001	0.021	3.469	1.204–9.993
	Blast cell proportion on the 15th day of induction therapy	0.025	0.154	1.676	0.825–3.407
	Extramedullary infiltration before HSCT	0.033	0.502	1.449	0.491–4.282
DFS	Age	0.004	0.455	1.360	0.607–3.048
	T-ALL	0.000	0.045	2.339	1.021–5.362
	LDH at diagnosis	0.000	0.024	3.426	1.172–10.016
	Blast cell proportion on the 15th day of induction therapy	0.006	0.098	1.812	0.897–3.661
	Extramedullary infiltration before HSCT	0.044	0.444	1.518	0.521–4.421

CI: Confidence interval; *RR*: Relative risk; OS: Overall survival; DFS: Disease-free survival; T-ALL: T-cell acute lymphoblastic leukemia; LDH: Lactic dehydrogenase; HSCT: Hematopoietic stem cell transplantation.

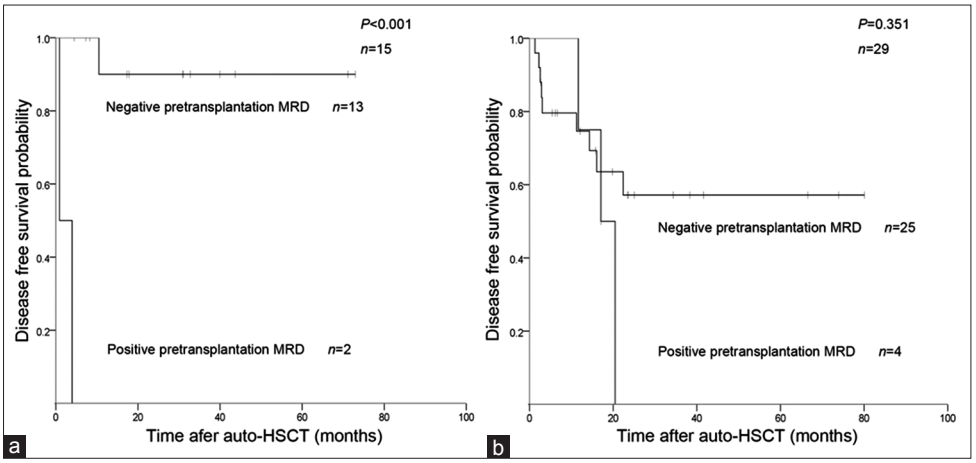

Figure 4: Disease-free survival (DFS) after auto-hematopoietic stem cell transplantation of patients with different pretransplantation minimal residual disease (a) DFS for standard-risk group; (b) DFS for high risk group.

donor was also acceptable. However, it is still uncertain which method is better for the patients without a suitable donor, the conventional chemotherapy or the auto-HSCT. Most studies showed no advantage for auto-HSCT compared with chemotherapy. However, this retrospective analysis of adult patients with ALL who underwent auto-HSCT in our center showed an encouraged outcome which was better than most reports. The reasons were chiefly as follows.

First, all the patients received "*in vivo* purging" with potent 4–10 courses consolidation chemotherapy in order to obliterate the malignant cells as many as possible. All the patients achieved CR prior to HSCT, and the most acquired pretransplantation MRD results of our study were negative. A retrospective analysis of 149 adult ALL patients who underwent allo-HSCT suggested that patients with positive MRD after HSCT had poor prognosis (shorter OS and DFS), and those with positive pretransplantation MRD trended to have lower OS and DFS rates without statistically significant difference.[9] Ribera[10] showed that HR patients with continuous negative MRD after conventional chemotherapy can avoid HSCT, while for those with positive MRD, whether clinically SR or HR, HSCT was the best postconsolidation therapy. However, there was rare study estimated the pretransplantation MRD of ALL patients with auto-HSCT. In this study, the pretransplantation MRD tests for 44 patients were performed. The survival curves showed that both OS and DFS of patients with positive pretransplantation MRD were shorter than those with negative results ($P < 0.05$). Furthermore, the positive results of SR group also meant unfavorable prognosis. In the HR group, patients with positive pretransplantation MRD also had a trend of shorter OS and DFS. Further study is still needed because of the limited cases allotted. Therefore, pretransplantation MRD plays an important role in predicting the prognosis of auto-HSCT. For the SR patients with negative MRD, auto-HSCT can be a feasible choice when the patients are too worried about the serious side effects of allo-HSCT. The patients with positive results are preferable to have allo-HSCT when a suitable donor is available, which may reduce the probability of relapse.

Second, most patients had maintenance therapy for 1–1.5 years after HSCT, except 6 patients died from transplantation-related mortality and 8 suffered from early relapse (leukemia recurrence before stable hematopoiesis reconstitution). Powles *et al*.[11] reported a prospective study about 77 adult ALL patients who underwent auto-HSCT. The result showed that posttransplantation maintenance therapy could improve therapeutic efficacy with 53% OS, 50% DFS, and 42% relapse rate at 10 years. These were similar to our data. Some reports also showed that compare with chemotherapy alone, the auto-HSCT combined with maintenance therapy had longer OS and DFS, no matter to SR or HR patients.[12] Similarly, Sirohi *et al*.[13] and Mehta *et al*.[14] also found that maintenance chemotherapy after auto-HSCT could diminish the relapse rate as well as improve the prognosis. Hence, administering the maintenance therapy as a part of posttransplantation therapy was significant to our success.

Third, outcomes of Ph-positive ALL patients who received auto-HSCT in our center were not poor than Ph chromosome negative group. Ph-chromosome was present in 20–30% of adults with ALL,[3] and Ph-positive ALL was generally considered as a malignant disease with poor prognosis. Allo-HSCT was suggested to these patients by most hematologists.[15] However, some newly studies had reported that auto-HSCT can provide a favorable end for the adult patient without an available donor. Bassan *et al*.[16] prospectively studied 94 patients and found that auto-HSCT combined with maintenance chemotherapy had similar effects with allo-HSCT for adult Ph-positive ALL patients. Two cases from Böhm *et al*.[17] indicated that auto-HSCT could provide long-term survival without any maintenance chemotherapy or TKIs after transplantation. Another retrospective analysis indicated that there were no different ends between diverse sources of stem cells, no matter from the patients themselves or identical siblings or unrelated donors.[18] In this study, 15 adult Ph-positive ALL patients received auto-HSCT totally, and the median follow-up time was 19.8 months (range 5.7–203.2 months). Survival analysis showed that the outcome of Ph-positive ALL patients was similar to those without Ph chromosome, and the OS, DFS, and relapse rate at 3 years were 71.5 ± 12.2%, 68.4 ± 13.2%, and 28.5 ± 1.6%, respectively. The reasons may be that we had gained some experience when most Ph-positive ALL patients received their auto-HSCT (13 patients received transplantation after 2006) and TKIs-the targeted therapeutic agents played an important role during the pretransplantation chemotherapy and posttransplantation maintenance therapy for most patients (13/15).

In this study, univariate analysis showed that T-ALL, high LDH at diagnosis, age ≥35 years, blast cell proportion ≥5% on the 15th day of induction therapy, and extramedullary infiltration before HSCT were the poor prognosis factors. In Cox regression model, T-ALL and high LDH were the independent undesirable factors associated with OS and DFS. These factors were in accordance with those in many other reports. In addition, some analyses indicated that many other factors such as high initial WBC count, time to achieve CR1 >28 days, some cytogenetic abnormalities (such as t(9;22), t(4;11) and so on) and timing of transplantation at CR2/greater were also associated with poor prognosis.[19] In our center, all patients were administered in advance with a series of strict intensive chemotherapy and myeloablative conditioning regimen which regularly contained TBI in order to minimize the residual diseases before auto-HSCT. And the known pretransplantation MRD also inferred that most patients had good "*in vivo* purging" before refusion. These may lead to indiscrimination between patients with and without high WBC count. Meanwhile, the patients whose time to achieve CR1 >28 days (12/135) or who had t(4;11) abnormality (3/135) or who underwent HSCT at CR2/greater (13/135) were only a small portion in the

cohort. As a consequence, these factors didn't influence the prognosis statistically in this study.

About the mobilization, we found a phenomenon that more than 4 courses consolidation chemotherapy before mobilization may make stem cell harvest more difficult. Among the 100 patients who received peripheral blood stem cell transplantation, 5 patients failed first mobilization, and all the 5 patients were mobilized after 5 (contain 5) courses consolidation chemotherapy. Hence, the success rate may higher when the patients received no more than 4 courses consolidation before collection (all the 47 patients won the first mobilization war, while success rate of the other 53 patients who were mobilized after 5 courses was 90.6%, $P = 0.031$). In the 6 patients whose stem cells came from BM and peripheral blood, 4 patients' mobilizations were performed after 5 or 6 courses consolidation chemotherapy, and the other 2 patients were mobilized after the 4th. Because of the failed mobilization from peripheral blood, more stem cells were harvested from BM. This was in accordance with other reports.[20]

In conclusion, auto-HSCT combined with maintenance therapy was an option when suitable donors were unavailable. For the SR patients who did not have any poor prognosis factors, such as T-ALL and high LDH at diagnosis, auto-HSCT combined with maintenance therapy would provide long survival when their pretransplantation MRD were negative.

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