Prognosis of patients with core binding factor acute myeloid leukemia after first relapse

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ABSTRACT

Core binding factor acute myeloid leukemia is known to have a favorable prognosis, however, there have been no detailed analyses on prognostic factors after first relapse. Using a nationwide database, we retrospectively analyzed core binding factor acute myeloid leukemia patients who relapsed after being treated with chemotherapy alone during their first complete remission. Of a total of 397 patients who were diagnosed with core binding factor acute myeloid leukemia, 208 experienced a first relapse, and analyses were performed in 139 patients for whom additional data were available. In the entire cohort, the overall survival rate after relapse was 48% at 3 years. By multivariate analysis, younger age at diagnosis, a longer interval before relapse, and inv(16) were shown to be independently associated with better survival after relapse. Although there was no significant difference in survival after relapse between patients who underwent allogeneic hematopoietic cell transplantation and those who did not in the overall series of relapsed patients, we found that transplantation significantly improved survival among patients who had t(8;21) (54% *versus* 26% at 3 years, P=0.002). In addition, among patients with t(8;21), those who had different cytogenetics at relapse had a significantly improved survival after transplantation, while those who had same cytogenetics did not. We showed that the prognosis differs significantly and optimal treatment strategies may vary between groups of patients with core binding factor acute myeloid leukemia with different cytogenetic profiles at relapse. These findings may help to guide therapeutic decisions after first relapse.

Introduction

Core binding factor acute myeloid leukemia [CBF-AML: (inv(16)/t(16;16)/del(16q) or t(8;21)] is considered to have a favorable/good risk according to existing cytogenetic classifications, including Southwest Oncology Group (SWOG) criteria,[1] Medical Research Council (MRC) criteria,[2,3] and Cancer and Leukemia Group B (CALGB).[4] These forms of leukemia are not, therefore, usually considered to be candidates for allogeneic hematopoietic cell transplantation (HCT) in first complete remission (CR1).[1,2,5,6] However, previous studies have reported a relapse incidence of 25-58%[3,7-9] in CBF-AML treated with chemotherapy alone, which demonstrates that a substantial number of patients with CBF-AML eventually require salvage treatment. Although several studies have tried to identify the factors that predict the outcome after relapse in AML patients,[10-15] little is known about the impact of either the clinical characteristics of CBF-AML at the time of relapse or the treatment strategies adopted after relapse. Although high-dose cytarabine has been shown to prolong the remission duration and improve the prognosis, especially in patients with CBF-AML,[16-18] a benefit of high-dose cytarabine after first relapse has not been evaluated. We previously showed that patients with CBF-AML who achieved a second complete remission (CR2) had comparable survival outcomes regardless of whether they did or did not receive salvage allogeneic HCT.[9] However, detailed analyses on clinical data, including cytogenetics at the time of relapse, and salvage treatment after relapse were not performed because of the lack of data. To address this issue and clarify the optimal treatment strategies for relapsed CBF-AML, we retrospectively analyzed CBF-AML patients who had their

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first relapse after being treated with chemotherapy alone during CR1.

Methods

Patients

Adults with AML who had achieved CR1 were retrospectively registered in a nationwide AML database, which formed the basis of this study.[6,9] This database included patients who were between 16 and 70 years of age, were diagnosed with AML between 1999 and 2006 according to the World Health Organization classification, and had achieved CR with one or two courses of chemotherapy. Seventy institutions contributed patients to the database. In the original database, information was collected on patient-related factors (e.g., age, sex), disease-related factors [e.g., cytogenetics, white blood cell (WBC) count at diagnosis], and clinical outcome including the date of relapse and achievement of CR2. For patients who underwent allogeneic HCT after relapse, complementary information on HCT (e.g., interval from relapse to HCT, disease status at the time of HCT, conditioning regimen, and donor source) was also collected. To perform this current study, supplementary information was collected for CBF-AML patients who had their first hematologic relapse. Additional data collected concerned cytogenetics and WBC count at first relapse, chemotherapy regimen adopted after the first relapse, and response to the initial treatment after the first relapse. Chromosome analysis was performed on metaphases from samples of bone marrow using standard banding techniques. Karyotypes were determined according to the International System for Human Cytogenetic Nomenclature. The cytogenetic data at relapse were centrally reviewed by a doctor who specialized in chromosome analysis, and classified into 'same cytogenetics' or 'different cytogenetics' from those at diagnosis. We categorized the "different cytogenetics" into three groups: decrease in cytogenetic abnormalities, increase in cytogenetic abnormalities, and unrelated change. A decrease or increase in cytogenetic abnormalities was defined as different chromosomal karyotypes harboring the original CBF-associated abnormality. Unrelated change was defined as a chromosomal karyotype that lost the original CBF-associated abnormality. The increase in cytogenetic abnormalities was further subdivided into two groups: numerical changes [e.g., 46,XY,inv(16)(p13;q22) → 47,XY,inv(16)(p13q22),+22] and structural changes [e.g., 46,XX,t(8;21)(q22;q22) → 46,XX,t(8;21)(q22;q22), t(9;10)(q34;q11)]. This study was approved by the Institutional Review Board at the National Cancer Centre Hospital.

Statistical analysis

Data were retrospectively reviewed and analyzed as of March 2012. Distributions of patients' characteristics between groups were compared using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. A Kaplan-Meier survival analysis was performed to estimate the probabilities of overall survival, which was defined as the time from the first relapse to death or the last visit. Differences in overall survival between groups were compared by means of the log-rank test. To compare the outcomes of patients who received allogeneic HCT after relapse and those who did not, we performed landmark analyses by excluding patients who died within 120 days from relapse. The Cox regression model was used to estimate hazard ratios (HR) and 95% confidence intervals (CI). As covariates considered in univariate and multivariate analyses, we selected clinically important factors that were present at the first relapse. All statistical analyses were performed with SPSS software version 11.0.1 (SPSS, Chicago, IL, USA) and EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing).

Results

Characteristics of relapsed patients

Of the total of 2516 patients, 397 were diagnosed with CBF-AML. Twenty-six patients underwent allogeneic HCT during CR1 [17 patients with t(8;21) and 9 with inv(16)]. Among the 371 patients who were treated with chemotherapy alone during the CR1, 208 (56%) experienced a first hematologic relapse, and analyses were performed in 139 [92 patients with t(8;21) and 47 with inv(16) including three with t(16;16)] for whom additional data were available (Figure 1). When compared using the characteristics obtained in the original database including overall survival after relapse, there was no difference in characteristics or overall survival between the 139 patients who were analyzed and the 69 for whom additional data were not available. The characteristics of the 139 relapsed patients are summarized according to cytogenetics [i.e., inv(16) *versus* t(8;21)] in Table 1. The median age of the relapsed patients was 47 years (range, 16-70). The median interval from CR1 to relapse was 284 days (range, 24-1948), and there was no difference between the two cytogenetic groups.

We investigated the cytogenetic profile at relapse in comparison with that at diagnosis. Cytogenetic data were not available for 10% of the patients because of an insufficient count of mitotic cells or because a chromosome analysis was not performed at relapse. Different cytogenetics were observed in 36% and 28% of those with t(8;21) and inv(16), respectively, and included a decrease in cytogenetic abnormalities (1% and 6%), an increase in cytogenetic abnormalities: numerical change (0% and 11%), an increase in cytogenetic abnormalities: structural change (21% and 0%), and unrelated changes (14% and 11%).

Therapeutic strategies and response after relapse

Online Supplementary Table S1 and Figure 1 show the

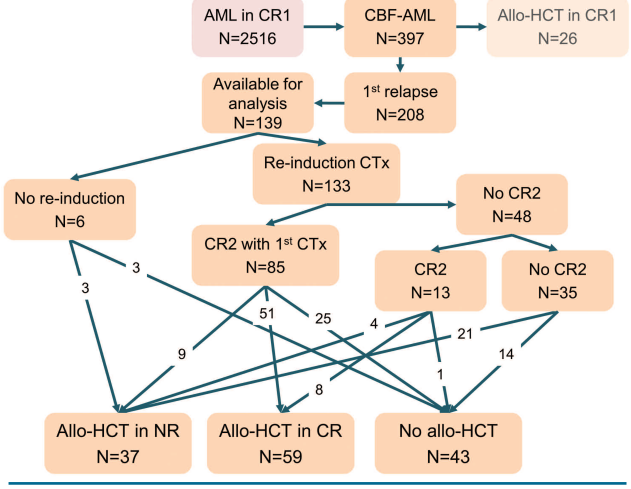

Figure 1. Flow diagram of patients. Allo-HCT: allogeneic hematopoietic cell transplantation; Ctx: chemotherapy; NR: non-remission; CR: complete remission.

treatments adopted after the first relapse. Six patients did not receive re-induction chemotherapy after relapse. Three of them underwent allogeneic HCT in non-remission and the other three died within 1 year without undergoing allogeneic HCT. As the first re-induction chemotherapy, standard-dose cytarabine-based therapy was given to 66% of the total population, and 21% patients received high-dose cytarabine-based treatment (i.e., 2 g/m^2 per dose or more). About 80% of those who received re-induction therapy continued cytarabine-based consolidation chemotherapy by the physicians' discretion. The rate of achievement of CR2 after the first re-induction therapy was 64%, and eventually 74% of those who were treated with chemotherapy after relapse achieved CR2. There was no significant difference in the rate of achievement of CR2 between those who received standard-dose cytarabine or high-dose cytarabine as the first therapy (standard-dose cytarabine, 68%; high-dose cytarabine, 59%; less-intensive chemotherapy, 42%). Although there was no difference in the proportions of re-induction regimens chosen in the two cytogenetic groups, those with inv(16) were significantly more likely to achieve CR2 with the first re-induction therapy (52% *versus* 79%, P=0.003). Only six patients underwent autologous HCT after relapse.

Table 1. Patients' characteristics.

	t(8;21) N=92	inv(16) N=47
Age		
Median, years (range)	43 (17-70)	51 (16-68)
Gender		
Male, n. (%)	60 (65)	32 (68)
Female, n. (%)	32 (35)	15 (32)
French-American-British classification		
M0, n. (%)	0 (0)	0 (0)
M1, n. (%)	2 (2)	3 (6)
M2, n. (%)	86 (93)	11 (23)
M4, n. (%)	2 (2)	33 (70)
M5, n. (%)	1 (1)	0 (0)
M6, n. (%)	0 (0)	0 (0)
M7, n. (%)	0 (0)	0 (0)
Others, n. (%)	1 (1)	0 (0)
WBC at diagnosis		
Median, 10^9/L (range)	10.8 (1.7-134.4)	56.5 (0.7-281.2)
WBC at relapse		
Median, 10^9/L (range)	3.2 (0.9-22.6)	2.9 (1.0-247.8)
Cytogenetics at relapse		
Same cytogenetics, n. (%)	51 (55)	27 (57)
Different cytogenetics, n. (%)	33 (36)	13 (28)
Decrease in abnormalities, n. (%)*	1 (1)	3 (6)
Increase in abnormalities		
Numerical change, n. (%)**	0 (0)	5 (11)
Structural change, n. (%)***	19 (21)	0 (0)
Unrelated change, n. (%)	13 (14)	5 (11)
No available data, n. (%)	8 (9)	7 (15)
Interval from CR1 to relapse		
Median, days (range)	278 (26-1948)	302 (24-1350)

CR1: first complete remission
** 44,XX,t(4;17)(p16;q11,2),inv(16)(p13q22) → 46,XX,inv(16)(p13q22)*
*** 46XY,inv(16)(p13q22) → 46XY,inv(16)(p13q22),+22*
**** 46,XX,t(8;21)(q22;q22) → 46,XX,t(8;21)(q22;q22),t(9;10)(q34;q11)*

Salvage allogeneic hematopoietic cell transplantation after relapse

Of the 139 relapsed patients, 96 (69%), who accounted for 71% and 66% of those with t(8;21) and inv(16), respectively, underwent allogeneic HCT after the first relapse (Table 2). The median age of those who underwent allogeneic HCT was 40 years (range, 16-66), which was significantly younger than that of the 43 patients who did not undergo allogeneic HCT (56 years, P<0.001). The interval from relapse to allogeneic HCT was 149 days, and allogeneic HCT was performed during CR2 in 57% of those who underwent salvage allogeneic HCT. The transplant was from an unrelated donor in 64% of cases, and a myeloablative conditioning regimen was used in 73% of the total population who underwent allogeneic HCT after relapse.

Overall survival after the first relapse

The median follow-up of surviving patients was 38 months from relapse, and the 3-year overall survival rate after relapse was 48% for the whole group of relapsed

Table 2. Characteristics of allogeneic hematopoietic cell transplantation after relapse.

	Total N=96	t(8;21) N=65	inv(16) N=31
Age, years			
Median, years (range)	40 (16-66)	35 (17-66)	44 (16-65)
Sex			
Male, n. (%)	62 (65)	39 (60)	23 (74)
Female, n. (%)	34 (35)	26 (40)	8 (26)
Cytogenetics at relapse			
Same cytogenetics, n. (%)	53 (55)	37 (57)	16 (52)
Different cytogenetics, n. (%)	29 (30)	21 (32)	8 (26)
Decrease in abnormalities, n. (%)	5 (5)	3 (5)	2 (6)
Increase in abnormalities			
Numerical change, n. (%)	5 (5)	0 (0)	5 (16)
Structural change, n. (%)	12 (13)	12 (18)	0 (0)
Unrelated change, n. (%)	9 (9)	6 (9)	3 (10)
No available data, n. (%)	12 (13)	7 (11)	5 (16)
WBC count at relapse			
Median, x10^9/L (range)	3.0 (0.9-248.8)	3.0 (0.9-13.0)	3.0 (1.0-248.8)
Interval from relapse to HCT			
Median, days (range)	149 (34-943)	148 (34-910)	181 (62-943)
Disease status at HCT			
CR2, n (%)	55 (57)	36 (55)	19 (61)
Beyond CR3, n. (%)	4 (4)	1 (2)	3 (10)
Non-remission after chemotherapy, n. (%)	23 (24)	18 (28)	5 (16)
Beyond 2nd relapse, n. (%)	11 (11)	7 (11)	4 (13)
No treatment, n. (%)	3 (3)	3 (5)	0 (0)
Donor			
Related, HLA matched, n. (%)	27 (28)	20 (31)	7 (23)
Related, HLA one-antigen mismatched, n. (%)	5 (5)	4 (6)	1 (3)
Unrelated, bone marrow, n. (%)	45 (47)	30 (46)	15 (48)
Unrelated, cord blood, n. (%)	16 (17)	9 (14)	7 (23)
Others or unknown, n. (%)	3 (3)	2 (3)	1 (3)
Conditioning			
Myeloablative, n. (%)	70 (73)	49 (75)	21 (68)
Reduced-intensity, n. (%)	24 (25)	14 (22)	10 (32)
Not specified, n. (%)	2 (2)	2 (3)	0 (0)

CR2: second complete remission; CR3: third complete remission.

patients with CBF-AML (Figure 2A). Patients with inv(16) had a better overall survival rate after relapse compared to those with t(8;21) (57% *versus* 43% at 3 years after relapse, *P*=0.022, Figure 2B). Patients' age at diagnosis (49 years or younger, 57%; 50 years or older, 34%, *P*=0.002, Figure 2C) and the interval from CR1 to relapse (≥365 days, 71%; <365 days, 35%, *P*<0.001, Figure 2D) significantly affected overall survival after relapse. With regards to the changes in cytogenetics at relapse, we divided patients into two groups: those who had an increase in structural abnormalities (n=19), and those who had either the same cytogenetics or other changes (n=105). We excluded the 15 patients for whom data were not available. Patients who had an increase in structural abnormalities had a significantly worse overall survival than those with the same cytogenetics or other changes (35% *versus* 51%, *P*<0.001, Figure 2E). We also found that a higher WBC count at relapse was associated with a worse survival rate after relapse (WBC ≤5x10^9/L, 54% *versus* WBC>5x10^9/L, 35%, *P*=0.041). However, the WBC count at diagnosis did not affect the outcome of CBF-AML after relapse. We also compared the outcomes on the basis of treatment adopted after relapse. There was no difference in overall survival between patients who received standard-dose cytarabine and those who received high-dose cytarabine (standard-dose cytarabine, 49%; high-dose cytarabine, 60%, *P*=0.257, Figure 2F). When the analysis was limited to the patients who have t(8;21), those who received high-dose cytarabine had a significantly better overall survival after relapse (37% *versus* 65%, *P*=0.036). We also looked at the effect of high-dose cytarabine given at any point after relapse. There was no difference in overall survival between patients who received high-dose cytarabine (n=64) and those who did not (n=75, 52% *versus* 43%, *P*=0.247). Achievement of CR2 after the first re-induction chemotherapy significantly improved the outcome after relapse (62% *versus* 23%, *P*<0.001, Figure 2G).

We performed a landmark analysis to compare overall survival after relapse in patients who underwent allogeneic HCT at any time after relapse and those who did not.

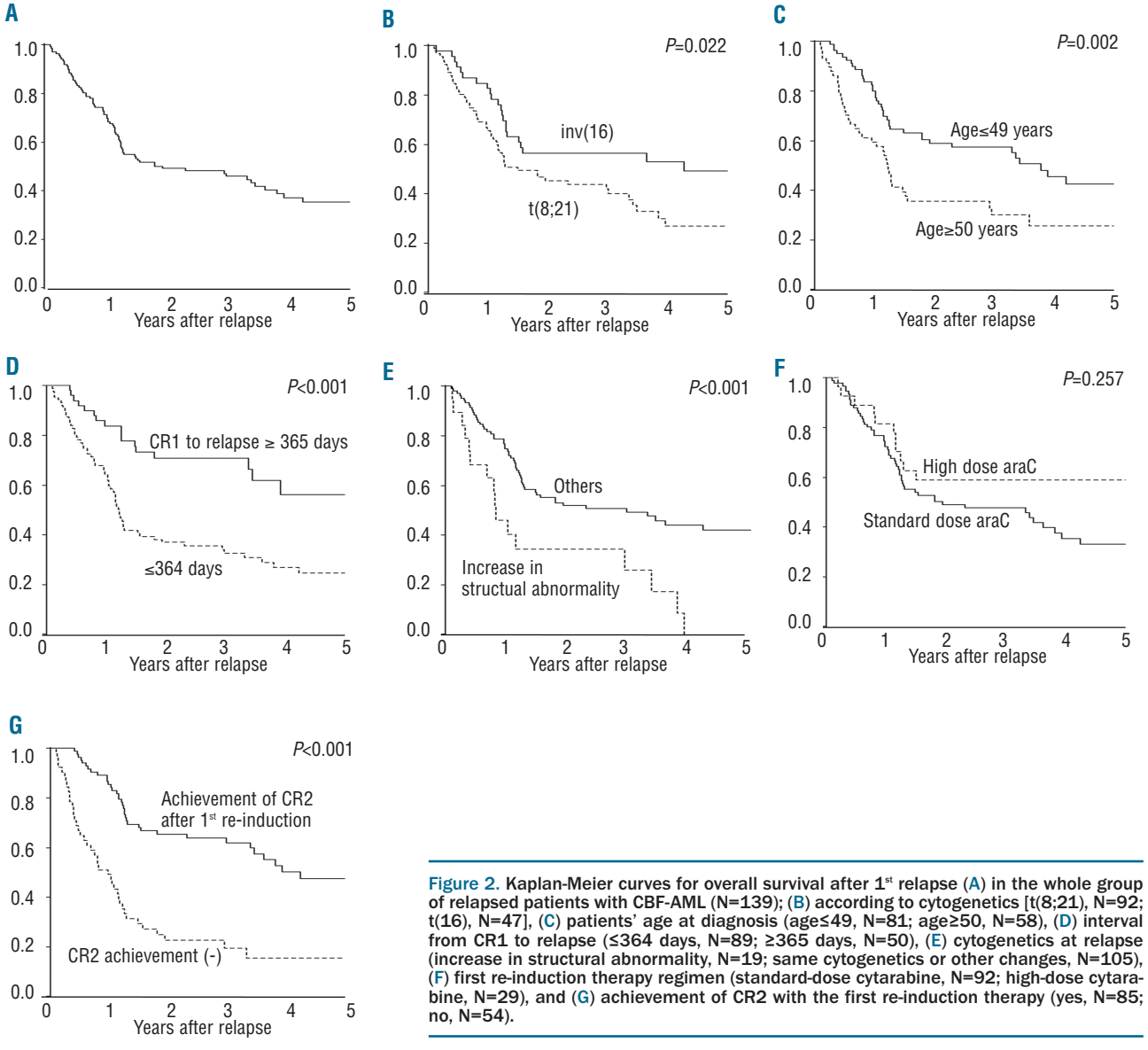

Figure 2. Kaplan-Meier curves for overall survival after 1st relapse (A) in the whole group of relapsed patients with CBF-AML (N=139); (B) according to cytogenetics [t(8;21), N=92; t(16), N=47], (C) patients' age at diagnosis (age≤49, N=81; age≥50, N=58), (D) interval from CR1 to relapse (≤364 days, N=89; ≥365 days, N=50), (E) cytogenetics at relapse (increase in structural abnormality, N=19; same cytogenetics or other changes, N=105), (F) first re-induction therapy regimen (standard-dose cytarabine, N=92; high-dose cytarabine, N=29), and (G) achievement of CR2 with the first re-induction therapy (yes, N=85; no, N=54).

The landmark analysis at 120 days excluded ten patients who died within 120 days of the date of relapse. The 3-year overall survival after relapse was 55% in 95 patients who underwent allogeneic HCT after relapse and 42% among 34 who did not (*P*=0.127, Figure 3A). Among patients who had t(8;21), the overall survival rate of those who underwent allogeneic HCT was significantly higher than that of patients who did not (54% *versus* 26% at 3 years after relapse, *P*=0.002, Figure 3B). In contrast, in patients who had inv(16), there was no difference in the overall survival rates between those who underwent allogeneic HCT and those who did not (57% *versus* 60%, *P*=0.901, Figure 3C). We further looked at the benefit of allogeneic HCT in patients with t(8;21) based on cytogenetic profile at relapse. In patients with t(8;21) who had different cytogenetics at relapse, the overall survival rate was significantly higher in those who underwent allogeneic HCT than in those who did not (56% *versus* 0%, *P*=0.022, Figure 3D). However, those who had same cytogenetics did not have a clear benefit from allogeneic HCT after relapse (54% *versus* 46%, *P*=0.148, Figure 3E). We found that overall survival did not differ significantly in regard to donor source (related *versus* unrelated bone marrow *versus* unrelated cord blood) or conditioning (myeloablative *versus* reduced-intensity).

Multivariate analysis for overall survival after the first relapse

Table 3 shows the results of univariate and multivariate analyses for overall survival after relapse. In a univariate analysis that considered clinically important factors which were present at the first relapse, a younger age at diagnosis, a longer interval from CR1 to relapse, the absence of an increase in structural abnormalities, and a WBC count of $5x10^9$/L or less at relapse were each shown to be significantly associated with better overall survival. In multivariate analysis, patients' age and the interval from CR1 to relapse remained statistically significant, and t(8;21) compared to inv(16) was shown to be independently associated with worse overall survival after relapse. Cytogenetics at first relapse (increase in structural abnormality *versus* others) was excluded from the initial model of multivariate analysis because of the interaction with cytogenetic profile at diagnosis [inv(16) *versus* t(8;21)]: an increase in structural abnormality was observed only in patients with t(8;21), therefore, either of cytogenetics at relapse or at diagnosis needed to be excluded from multivariate analysis. When we replaced cytogenetic profile at diagnosis with cytogenetics at first relapse, increase in structural abnormality was shown to be an independent prognostic factor associated with worse overall survival. We also looked at the effect of allogeneic HCT after relapse by adding performance of allogeneic HCT as a time-dependent covariate in a multivariate analysis. Allogeneic HCT after relapse was not an independent prognostic factor by multivariate analysis, which was in line with the landmark analysis in the patients as a whole. In addition, the regimen of initial reinduction chemotherapy (standard *versus* high-dose cytarabine) was not shown to be significantly associated

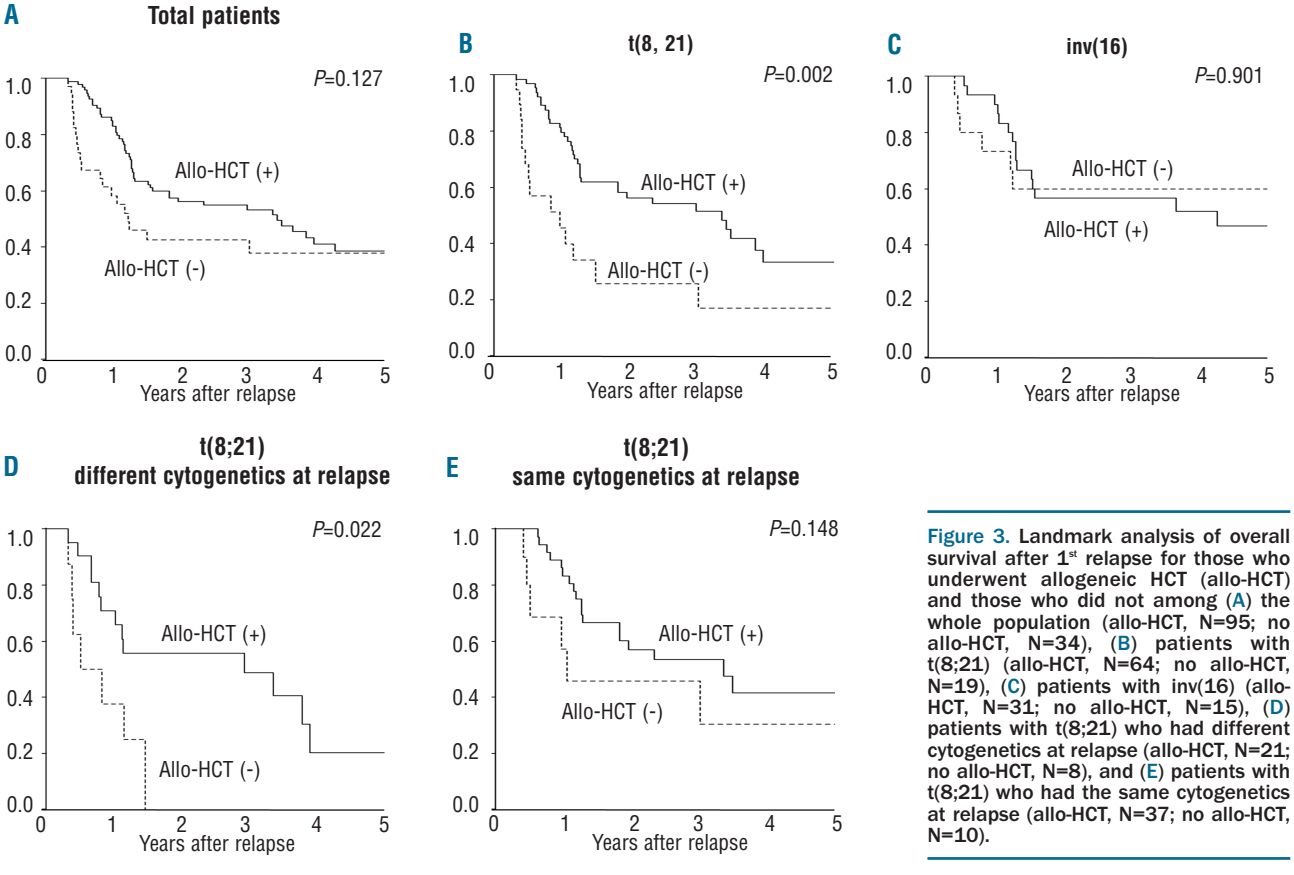

Figure 3. Landmark analysis of overall survival after 1st relapse for those who underwent allogeneic HCT (allo-HCT) and those who did not among (A) the whole population (allo-HCT, N=95; no allo-HCT, N=34), (B) patients with t(8;21) (allo-HCT, N=64; no allo-HCT, N=19), (C) patients with inv(16) (allo-HCT, N=31; no allo-HCT, N=15), (D) patients with t(8;21) who had different cytogenetics at relapse (allo-HCT, N=21; no allo-HCT, N=8), and (E) patients with t(8;21) who had the same cytogenetics at relapse (allo-HCT, N=37; no allo-HCT, N=10).

with overall survival after relapse when added in the initial model of multivariate analysis.

Discussion

Using a nationwide database of adult AML patients who achieved CR1, we retrospectively analyzed CBF-AML patients who had their first hematologic relapse after being treated with chemotherapy alone, to evaluate the impact of the clinical characteristics of CBF-AML at the time of relapse on the outcome. We previously showed that patients with CBF-AML had comparable survival outcomes whether or not they underwent allogeneic HCT after achieving CR2.[9] In this additional study, we showed that the effect of allogeneic HCT after relapse differs between patients with t(8;21) and those with inv(16), and optimal treatment strategies may vary between the two cytogenetic groups.

In this study, we examined the cytogenetic profile at relapse in comparison with that at diagnosis. We found that patients who had an increase in structural abnormalities at relapse had a significantly worse overall survival than other patients. Interestingly, among those who had different cytogenetic abnormalities, an increase in structural abnormality was observed only in patients with t(8;21). This inferior outcome of patients who had an increase in structural abnormalities in the t(8;21) group may have influenced the difference in prognosis after relapse between patients with t(8;21) and those with inv(16).

In the whole group of patients with CBF-AML who relapsed, the overall survival rate was 48% at 3 years after relapse, which was better than the previously reported overall survival of 30% after relapse of non-M3 AML.[9] By multivariate analysis, we found that an age of 49 years or younger at diagnosis, a longer interval from CR1 to relapse, and harboring inv(16) were associated with better outcome after relapse. Patients' age and relapse-free interval were shown to affect the outcome of patients with recurrent or relapsed AML in a prior study that investigated the prognosis of non-M3 AML after relapse.[11] Older age was also reported to be an independent factor that predicted shorter survival after relapse in a prior study[15] that analyzed prognostic factors of CBF-AML.

In this study, we showed that patients with t(8;21) had a significantly inferior prognosis compared to those with inv(16), as had been reported in prior studies.[7,8,11,15] In addition, we found other differences between the two cytogenetic groups regarding prognosis based on the treatment strategies after relapse. Although the effect of high-dose cytarabine as a consolidation therapy after CR1 has been shown,[16-18] we did not find a remarkable difference in overall survival between those who received standard-dose or high-dose cytarabine after relapse. However, in an analysis limited to patients with t(8;21), those who received high-dose cytarabine as the first re-induction therapy had a significantly improved overall survival. The impact of high-dose cytarabine intensification in patients with CBF-AML after relapse needs to be evaluated in more detail in an analysis of a larger number of patients.

We previously indicated that, in patients with relapsed CBF-AML, there was no significant difference in overall survival after relapse between those who did or did not undergo allogeneic HCT in CR2.[9] In this additional study, allogeneic HCT did not significantly improve overall survival among the whole group of patients with relapsed CBF-AML. However, in patients who had t(8;21), those who underwent allogeneic HCT had a significantly improved overall survival compared to those who did not. In contrast, in patients who had inv(16), those who did and did not receive allogeneic HCT had comparable overall survival rates of about 60% at 3 years after relapse. Additionally, in a further analysis based on cytogenetic profile at relapse, we found that those with t(8;21) who had different cytogenetics at relapse had a significantly improved overall survival when they underwent allogeneic HCT after relapse, but those who had the same cytogenetics did not show a benefit from allogeneic HCT. The evaluation of minimal residual disease detected by molecular markers may further stratify treatment strategies for patients with relapsed CBF-AML[19,20] especially among those who did not derive an apparent benefit from allo-

Table 3. Factors associated with survival after 1st relapse.

	Univariate analysis			Multivariate analysis		
	HR	(95% CI)	*P* value	HR	(95% CI)	*P* value
Gender						
Male	1			1		
Female	0.69	(0.43-1.11)	0.123	0.87	(0.51-1.49)	0.617
Age						
49 years or younger	1			1		
50 years or older	2.09	(1.34-3.24)	0.001	2.33	(1.39-3.88)	0.001
Interval from CR1 to relapse						
As a numerical variable (per 30 days)	0.92	(0.89-0.96)	<0.001	0.94	(0.90-0.98)	0.003
Cytogenetics at diagnosis						
inv(16)	1					
t(8;21)	1.62	(1.00-2.62)	0.051	2.25	(1.29-3.94)	0.004
Cytogenetics at 1st relapse						
Other than increase in structural abnormalities	1					
Increase in structural abnormalities	1.96	(1.09-3.52)	0.026			
WBC count at relapse						
$5x10^9$/L or less	1			1		
More than $5x10^9$/L	1.76	(1.06-2.95)	0.031	1.66	(0.95-2.90)	0.078

HR: hazard ratio; CI: confidence interval.

geneic HCT after relapse. In addition, genetic profile, including *KIT* mutation, in patients with CBF-AML may help to guide therapeutic decisions not only in first complete remission but also after first relapse.[21-23] The impact of cytogenetic profile at relapse on the benefit of allogeneic HCT needs to be evaluated in a study including a larger number of patients.

Our study has several limitations, and thus the results must be interpreted with caution. These limitations include the retrospective nature of the study including the fact that therapeutic strategies after relapse were chosen at the discretion of physicians, a lack of information regarding genetic profile, a lack of information regarding the presence of second relapse in those who did not undergo allogeneic HCT, and the relatively small number of patients analyzed. However, we showed that the prognosis differs significantly between groups of CBF-AML patients with different cytogenetic profiles at relapse. In addition, we found that optimal treatment strategies may vary between patients with t(8;21) and those with inv(16). These findings may help to guide therapeutic decisions including the indications for allogeneic HCT in patients with CBF-AML in first relapse. Further analyses using molecular profiling are warranted.

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Authorship and Disclosures

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