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Research Paper

High expression of MiR-98 is a good prognostic factor in acute myeloid leukemia patients treated with chemotherapy alone

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Abstract

It has been demonstrated that microRNA-98 (miR-98) is dysregulated in multiple types of solid tumors, but its expression and impact in acute myeloid leukemia (AML) is unclear. To explore the prognostic role of miR-98 in AML, 164 AML patients with the miR-98 expression data were extracted from The Cancer Genome Atlas (TCGA) database and enrolled in this study. First, patients were divided into chemotherapy-only (chemotherapy) group and allogeneic hematopoietic stem cell transplant (allo-HSCT) group. Each group was then divided in two groups by the median expression level of miR-98. In chemotherapy group, high miR-98 expression was associated with longer event-free survival (EFS, P = 0.003) and overall survival (OS, P = 0.004), but in allo-HSCT group, EFS and OS were not significantly different between high and low miR-98 expressers. Second, All patients were divided in two groups by the median expression level of miR-98. In low miR-98 expressers, those treated with allo-HSCT had longer EFS (P = 0.001) and OS (P < 0.001) than chemotherapy, but in high miR-98 expressers, survival was independent from treatment modalities. Gene ontology enrichment analysis indicated that the genes associated with miR-98 expression were mainly concentrated in "definitive hemopoiesis", "negative regulation of myeloid cell differentiation" and "signaling pathways regulating pluripotency of stem cells" pathways. In conclusion, our results indicated that high miR-98 expression confers good prognosis in AML patients treated with chemotherapy alone. Patients with low miR-98 expression may benefit from allo-HSCT.

Key words: Acute myeloid leukemia; MiR-98; Allogeneic hematopoietic stem cell transplantation; Chemotherapy; Prognosis

Introduction

The vast genetic heterogeneity is not only characteristic of acute myeloid leukemia (AML) [1] but also has important prognostic implications. For example, *NPM1* mutation without positive *FLT3-ITD* is a good prognostic factor in cytogenetically normal AML (CN-AML) [2,3], while the latter is a poor prognostic factor [4]. *DNMT3A* and *TP53* mutations are both negative prognostic factors in AML [5,6]. Double *CEBPA* mutation is associated with favorable prognosis in CN-AML patients [7].

MicroRNAs (miRNAs) are short noncoding RNAs that regulate genes post-transcriptionally and play an important role in various physiological and developmental processes such as cell proliferation and differentiation, development, and apoptosis, all of which are frequently affected in cancer [8,9]. Growing number of studies are demonstrating that the dysregulation of miRNAs is associated with the development and progression of many cancers including leukemia, and may provide useful prognostic information [10-13]. For instance, higher levels of miR-155 and lower levels of miR-181a are independently associated with shorter survival in CN-AML patients [14]. MiR-29a and miR-29b can induce apoptosis in AML by targeting apoptosis gene MCL-1 [15]. MiR-9 and miR-196b play essential oncogenic roles in mixed lineage leukemia-rearranged AML [16]. High miR-99a expression and low miR-215 expression are associated with worse clinical outcome in AML [17,18].

MiR-98 belongs to the let-7 families that have been shown to be down-regulated in high-risk ovarian cancer, lung cancer, melanoma and other solid tumors [19-22]. Previous study found that let-7b and let-7c were tumor suppressors and would be down-regulated in AML with t(8;21) or inv(16) [23]. Here, we retrospectively studied the association between miR-98 expression and survival in AML patients to help elucidating its clinical and prognostic implications.

Materials and Methods

Patients

A total of 164 AML patients with miR-98 expression data were identified in The Cancer Genome Atlas (TCGA) database (https://cancergenome.nih.gov/) and enrolled in this study [24]. Ninety patients were treated with chemotherapy alone, and other 74 also received allogeneic hematopoietic stem cell transplant (allo-HSCT). All clinical and molecular information including miR-98 expression levels were publicly accessible from the TCGA website. All patients provided written informed consent; the research was approved by the Human Research Ethics Committee of Washington University. Primary endpoints were event-free survival (EFS) and overall survival (OS). EFS was defined as the time from diagnosis to removal from the study due to the absence of complete remission, relapse or death or was censored at the last follow-up. OS was defined as the time from diagnosis to death or was censored at the last follow-up.

Statistical Analysis

All statistical analyses were performed by SPSS software 20.0 and GraphPad Prism software 5.0. The clinical and molecular characteristics of patients were summarized using descriptive statistics. The Mann-Whitney U test and the chi-square test were used to compare continuous and categorical data between the two groups, respectively. The EFS and OS rates were estimated using the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazard models were constructed for uni- and multivariate analyses to identify the association between each clinical and molecular variable and survival. For all statistical analyses, P values were two-sided and $P < 0.05$ was considered significant.

Results

Associations between miR-98 expression and clinical and molecular characteristics of patients

Patients were divided into two groups based on the treatment they received chemotherapy group and allo-HSCT group. Each group was then divided into two groups by the median expression level of miR-98. The clinical and molecular characteristics of each group were detailed in Table 1.

In the chemotherapy group, high miR-98 expressers had lower percentages of bone marrow (BM) blasts ($P = 0.048$), more good-risk patients ($P = 0.002$) and fewer intermediate-risk patients ($P = 0.011$) than low expressers. Six patients among the high expressers harbored *RUNX1-RUNX1T*, whereas it was not found in low expressers ($P = 0.026$). High expressers had less in *NPM1* ($P = 0.001$) and *DNMT3A* ($P = 0.002$) mutations. No significant differences were found in age, gender distribution, WBC counts, peripheral blood (PB) blasts, French-American-British (FAB) classification, frequency of other recurrent genetic mutations (*FLT3-ITD*, *CEBPA*, *IDH1*/*IDH2*, *RUNX1*, *MLL-PTD*, *TP53*, *NRAS*/*KRAS* and *TET2*) and relapse rate between high and low miR-98 expression groups.

In the allo-HSCT group, high miR-98 expressers had younger ($P = 0.043$), more poor-risk ($P = 0.047$), and fewer intermediate-risk patients ($P = 0.002$) than low expressers. High expressers had less *NPM1* ($P < 0.001$) and *DNMT3A* mutations ($P = 0.007$). No significant differences were found in gender distribution, BM blasts, FAB classification, karyotypes, frequency of other recurrent genetic mutations (*FLT3-ITD*, *CEBPA*, *IDH1*/*IDH2*, *RUNX1*, *MLL-PTD*, *NRAS*/*KRAS*, *TET2* and *TP53*) and relapse rate between high and low miR-98 expression groups.

Table 1. Clinical and molecular characteristics of patients in different treatment groups

Characteristics	Chemotherapy group			Allo-HSCT group		
	High miR-98 (n = 45)	Low miR-98 (n = 45)	*P*	High miR-98 (n = 37)	Low miR-98 (n = 37)	*P*
Age/years, median (range)	66 (22-88)	67 (31-83)	0.781*	45 (18-72)	56 (21-69)	0.043*
Age group/n (%)			0.822§			0.116§
< 60 years	14 (31.1)	15 (33.3)		30 (81.1)	24 (64.9)	
≥ 60 years	31 (68.9)	30 (66.7)		7 (18.9)	13 (35.1)	
Gender/n (%)			0.396§			0.159§
Male	27 (60.0)	23 (51.1)		24 (64.9)	18 (48.6)	
Female	18 (40.0)	22 (48.9)		13 (35.1)	19 (51.4)	
WBC/×10^9/L, median (range)	14 (1.0-131.5)	36 (0.7-298.4)	0.062*	29.4(1.2-223.8)	29.4(0.6-202.7)	0.510*
BM blast/%, median (range)	69 (30-91)	76 (32-99)	0.048*	71 (30-99)	75 (35-100)	0.210*
PB blast/%, median (range)	25 (0-97)	46 (0-98)	0.508*	48.5 (0-94)	45 (0-96)	0.699*
FAB subtypes/n (%)						
M0	2 (4.4)	6 (13.3)	0.266§	3 (8.1)	6 (16.2)	0.479§
M1	11 (24.4)	9 (20.0)	0.612§	11 (29.7)	12 (32.4)	0.802§
M2	14 (31.1)	7 (15.6)	0.081§	10 (27.0)	9 (24.3)	0.790§
M3	0 (0.0)	0 (0.0)		1 (2.7)	1 (2.7)	1.000§
M4	12 (26.7)	12 (26.7)	1.000§	9 (24.3)	5 (13.5)	0.235§
M5	5 (11.1)	8 (17.6)	0.368§	1 (2.7)	3 (8.1)	0.615§
M6	1 (2.2)	1 (2.2)	1.000§	1 (2.7)	0 (0.0)	1.000§
M7	0 (0.0)	2 (4.4)	0.494§	1 (2.7)	1 (2.7)	1.000§
Karyotype/n (%)						
Normal	18 (40.0)	26 (57.8)	0.092§	11 (29.7)	23 (62.2)	0.005§
Complex	7 (15.6)	5 (11.1)	0.535§	7 (18.9)	5 (13.5)	0.528§
8 Trisomy	0 (0.0)	0 (0.0)		3 (8.1)	3 (8.1)	1.000§
inv(16)/CBFβ-MYH11	6 (13.3)	1 (2.2)	0.110§	5 (13.5)	0 (0.0)	0.054§
11q23/MLL	3 (6.7)	0 (0.0)		2 (5.4)	1 (2.7)	1.000§
-7/7q-	0 (0.0)	3 (6.7)	0.242§	2 (5.4)	1 (2.7)	1.000§
t(15;17)/PML-RARA	0 (0.0)	0 (0.0)		1 (2.7)	1 (2.7)	1.000§
t(9;22)/BCR-ABL1	1 (2.2)	0 (0.0)	1.000§	2 (5.4)	0 (0.0)	0.493§
t(8;21)/RUNX1-RUNX1T1	6 (13.3)	0 (0.0)	0.026§	0 (0.0)	1 (2.7)	1.000§
Others	4 (8.9)	10 (22.2)	0.144§	4 (10.8)	2 (5.4)	0.674§
Risk/n (%)						
Good	12 (26.7)	1 (2.3)	0.002§	6 (16.7)	2 (5.4)	0.261§
Intermediate	19 (42.2)	31 (72.1)	0.011§	14 (38.9)	27 (73.0)	0.002§
Poor	14 (31.1)	11 (25.6)	0.480§	16 (44.4)	8 (21.6)	0.047§
***FLT3-ITD*/n (%)**			0.270§			0.782§
Positive	6 (13.3)	10 (22.2)		8 (21.6)	9 (24.3)	
Negative	39 (86.7)	35 (77.8)		29 (78.4)	28 (75.7)	
***NPM1*/n (%)**			0.001§			0.000§
Mutation	7 (15.6)	22 (48.9)		1 (2.7)	19 (51.4)	
Wildtype	38 (84.4)	23 (51.1)		36 (97.3)	18 (48.6)	
***CEBPA*/n (%)**			0.557§			0.305§
Single mutation	2 (4.4)	1 (2.2)		4 (10.8)	1 (2.7)	
Double mutation	0 (0.0)	0 (0.0)		2 (5.4)	1 (2.7)	
Wild type	43 (95.6)	44 (97.8)		31 (83.8)	35 (94.6)	
***DNMT3A*/n (%)**			0.002§			0.007§
Mutation	6 (13.3)	19 (42.2)		4 (10.8)	14 (37.8)	
Wildtype	39 (86.7)	26 (57.8)		33 (89.2)	23 (62.2)	
***IDH1/IDH2*/n (%)**			0.098§			0.104§
Mutation	11 (24.4)	5 (11.1)		6 (16.2)	12 (32.4)	
Wildtype	34 (75.6)	40 (88.9)		31 (83.8)	25 (67.6)	
***RUNX1*/n (%)**			1.000§			1.000§
Mutation	4 (8.9)	4 (8.9)		4 (10.8)	4 (10.8)	
Wildtype	41 (91.1)	41 (91.1)		33 (89.2)	33 (89.2)	
***MLL-PTD*/n (%)**			1.000§			0.615§
Presence	3 (6.7)	2 (4.4)		3 (8.1)	1 (2.7)	
Absence	42 (93.3)	43 (95.6)		34 (91.9)	36 (97.3)	
***NRAS/KRAS*/n (%)**			0.345§			0.430§
Mutation	8 (18.2)	5 (11.1)		2 (5.4)	5 (13.5)	
Wildtype	36 (81.8)	40 (88.9)		35 (94.6)	32 (86.5)	
***TET2*/n (%)**			1.000§			1.000§
Mutation	6 (13.3)	6 (13.3)		2 (5.4)	2 (5.4)	
Wildtype	39 (86.7)	39 (86.7)		35 (94.6)	35 (94.6)	
***TP53*/n (%)**			0.748§			1.000§
Mutation	6 (13.3)	5 (11.1)		2 (5.4)	2 (5.4)	

Characteristics	Chemotherapy group			Allo-HSCT group		
	High miR-98 (n = 45)	Low miR-98 (n = 45)	*P*	High miR-98 (n = 37)	Low miR-98 (n = 37)	*P*
Wildtype	39 (86.7)	40 (88.9)		35 (94.6)	35 (94.6)	
Relapse/n (%)			0.078§			1.000§
Yes	12 (26.7)	20 (44.4)		12 (32.4)	12 (32.4)	
No	33 (73.3)	25 (55.6)		25 (67.6)	25 (67.6)	

Abbreviations: WBC, white blood cell; BM, bone marrow; PB, peripheral blood; FAB, French American British. '*' denotes Mann-Whitney U test; '§' denotes chi-square test.

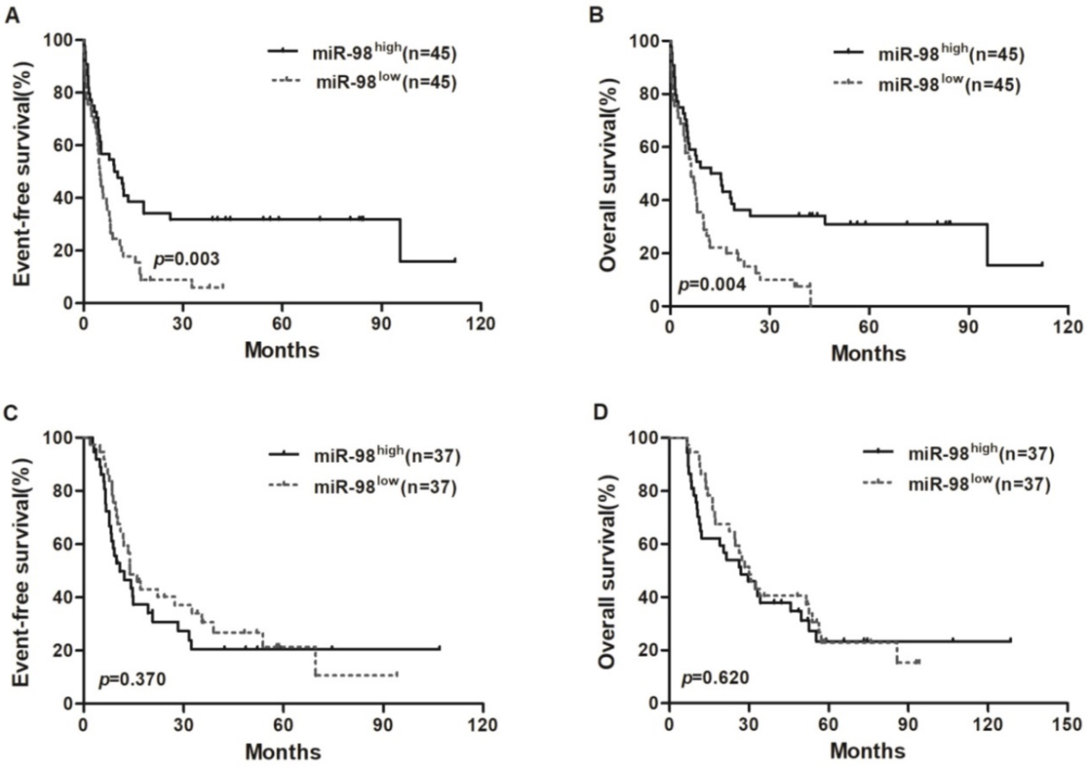

Figure 1. Kaplan-Meier curves of EFS and OS in chemotherapy group and allo-HSCT group. (A, B) In chemotherapy group, high miR-98 expressers had longer EFS and OS than low expressers. (C, D) EFS and OS were not significantly different between high miR-98 expression group and low expression group in allo-HSCT group.

Survival analysis of chemotherapy and allo-HSCT groups

Survival analyses were estimated using the Kaplan-Meier method. In chemotherapy group, high miR-98 expressers had a longer EFS ($P = 0.003$) and OS ($P = 0.004$; Figure 1A and 1B) compared with low expressers, but EFS and OS were not significantly different between high miR-98 expression group and low expression group in allo-HSCT group (Figure 1C and 1D).

Prognostic value of miR-98 expression

To assess the prognostic significance of clinical and molecular characteristics, we chose miR-98 expression levels (low vs. high), age (< 60 vs. ≥ 60 years), WBC counts ($< 20\times10^9$/L vs. $\geq 20\times10^9$/L), *FLT3-ITD* (positive vs. negative) and *NPM1* (mutated vs. wild), *DNMT3A* (mutated vs. wild) to do survival analysis.

In the chemotherapy group, univariate analysis indicated that low miR-98 expression and age ≥ 60 years were unfavorable for both EFS and OS (all $P < 0.01$). Multivariate analysis showed that low miR-98 expression and age ≥ 60 years were independent risk factors for both EFS and OS (all $P < 0.05$). WBC counts and other genetic abnormalities (*FLT3-ITD*, *NPM1*, *DNMT3A*) had no significant effect on EFS and OS (Table 2).

In the allo-HSCT group, univariate and multivariate analyses all indicated that miR-98 had no association with EFS and OS. Other clinical and molecular parameters also had no impact on EFS and OS in this group (Table 3).

In all patients, multivariate analysis indicated that allo-HSCT and age < 60 years were independent favorable factors for both EFS and OS (all $P < 0.05$) (Table 4).

Table 2. Uni- and multivariate analyses for EFS and OS in chemotherapy-only group

Variables	EFS		OS	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
Univariate analyses				
MiR-98 (high vs. low)	0.516 (0.321-0.829)	0.006	0.522 (0.324-0.841)	0.008
Age (< 60 vs. ≥ 60 years)	3.588 (2.005-6.421)	0.000	3.423 (1.919-6.106)	0.000
WBC (< 20 vs. ≥ 20×10^9/L)	1.037 (0.655-1.644)	0.876	1.068 (0.674-1.693)	0.779
FLT3-ITD (positive vs. negative)	1.261 (0.703-2.260)	0.436	1.192 (0.665-2.136)	0.555
NPM1 (mutated vs. wild type)	1.120 (0.687-1.827)	0.649	1.044 (0.640-1.704)	0.862
DNMT3A (mutated vs. wild type)	1.407 (0.852-2.322)	0.182	1.432 (0.868-2.362)	0.160
Multivariate analyses				
MiR-98 (high vs. low)	1.796 (1.041-3.100)	0.035	1.739 (1.005-3.009)	0.048
Age (< 60 vs. ≥ 60 years)	3.681 (2.036-6.657)	0.000	3.411 (1.889-6.158)	0.000
WBC (< 20 vs. ≥ 20×10^9/L)	1.190 (0.721-1.965)	0.496	1.160 (0.703-1.913)	0.562
FLT3-ITD (positive vs. negative)	0.893 (0.491-1.626)	0.712	1.035 (0.565-1.895)	0.913
NPM1 (mutated vs. wild type)	1.175 (0.647-2.133)	0.596	1.326 (0.726-2.420)	0.359
DNMT3A (mutated vs. wild type)	0.747 (0.423-1.320)	0.316	0.692 (0.399-1.201)	0.191

Abbreviations: EFS, event-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; WBC, white blood cell.

Table 3. Uni- and multivariate analyses for EFS and OS in allo-HSCT group

Variables	EFS		OS	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
Univariate analyses				
MiR-98 (high vs. low)	1.273 (0.749-2.163)	0.372	1.143 (0.673-1.941)	0.620
Age (< 60 vs. ≥ 60 years)	1.042 (0.581-1.868)	0.890	1.448 (0.807-2.599)	0.215
WBC (< 20 vs. ≥ 20×10^9/L)	0.754 (0.442-1.285)	0.299	0.985 (0.578-1.680)	0.956
FLT3-ITD (positive vs. negative)	1.719 (0.915-3.229)	0.092	1.588 (0.848-2.972)	0.148
NPM1 (mutated vs. wild type)	0.907 (0.494-1.666)	0.753	0.910 (0.495-1.671)	0.761
DNMT3A (mutated vs. wild type)	1.184 (0.643-2.178)	0.588	1.320 (0.715-2.438)	0.374
Multivariate analyses				
MiR-98 (high vs. low)	0.818 (0.437-1.533)	0.531	0.740 (0.392-1.400)	0.355
Age (< 60 vs. ≥ 60 years)	1.193 (0.637-2.232)	0.581	1.531 (0.820-2.860)	0.181
WBC (< 20 vs. ≥ 20×10^9/L)	1.372 (0.767-2.454)	0.286	1.075 (0.605-1.907)	0.806
FLT3-ITD (positive vs. negative)	0.529 (0.260-1.075)	0.078	0.559 (0.274-1.139)	0.109
NPM1 (mutated vs. wild type)	1.351 (0.630-2.896)	0.439	1.240 (0.579-2.654)	0.580
DNMT3A (mutated vs. wild type)	0.785 (0.410-1.506)	0.467	0.646 (0.333-1.255)	0.197

Abbreviations: EFS, event-free survival; OS, overall survival; Allo-HSCT, allogeneic hematopoietic stem cell transplantation; HR, hazard ratio; CI, confidence interval; WBC, white blood cell.

Table 4. Multivariate analyses for EFS and OS based on all patients

Variables	EFS		OS	
	HR (95%CI)	*P*-value	HR (95%CI)	*P*-value
MiR-98 (high vs. low)	1.405 (0.945-2.089)	0.093	1.465 (0.979-2.192)	0.064
Age (< 60 vs. ≥ 60 years)	2.254 (1.543-3.293)	0.000	2.358 (0.820-2.860)	0.000
WBC (< 20 vs. ≥ 20×10^9/L)	1.349 (0.927-1.963)	0.118	1.177 (0.811-1.709)	0.391
FLT3-ITD (positive vs. negative)	0.781 (0.502-1.215)	0.273	0.886 (0.565-1.389)	0.597
NPM1 (mutated v wild type)	1.240 (0.788-1.952)	0.352	1.327 (0.840-2.098)	0.226
DNMT3A (mutated v wild type)	0.731 (0.484-1.103)	0.136	0.685 (0.455-1.031)	0.070
Chemotherapy vs. allo-HSCT	1.459 (1.015-2.097)	0.041	1.765 (1.219-2.556)	0.003

Abbreviations: EFS, event-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; WBC, white blood cell; Allo-HSCT, allogeneic hematopoietic stem cell transplantation.

We also divided all patients into two groups based on median expression level of miR-98. In the low miR-98 expressers, allo-HSCT treatment were associated with longer EFS and OS than chemotherapy-alone ($P = 0.001$, $P < 0.001$, respectively; Figure 2A and 2B), but EFS and OS were not significantly different in high miR-98 expressers (Figure 2C and 2D).

Associations between genome-wide miRNA and gene-expression profiles and miR-98 expression

To further assess the role of miR-98 in AML, we derived miR-98-associated miRNA and gene expression profiles by high throughput sequencing from TCGA data. First, we found 251 up-regulated and 26 down-regulated miRNAs that were

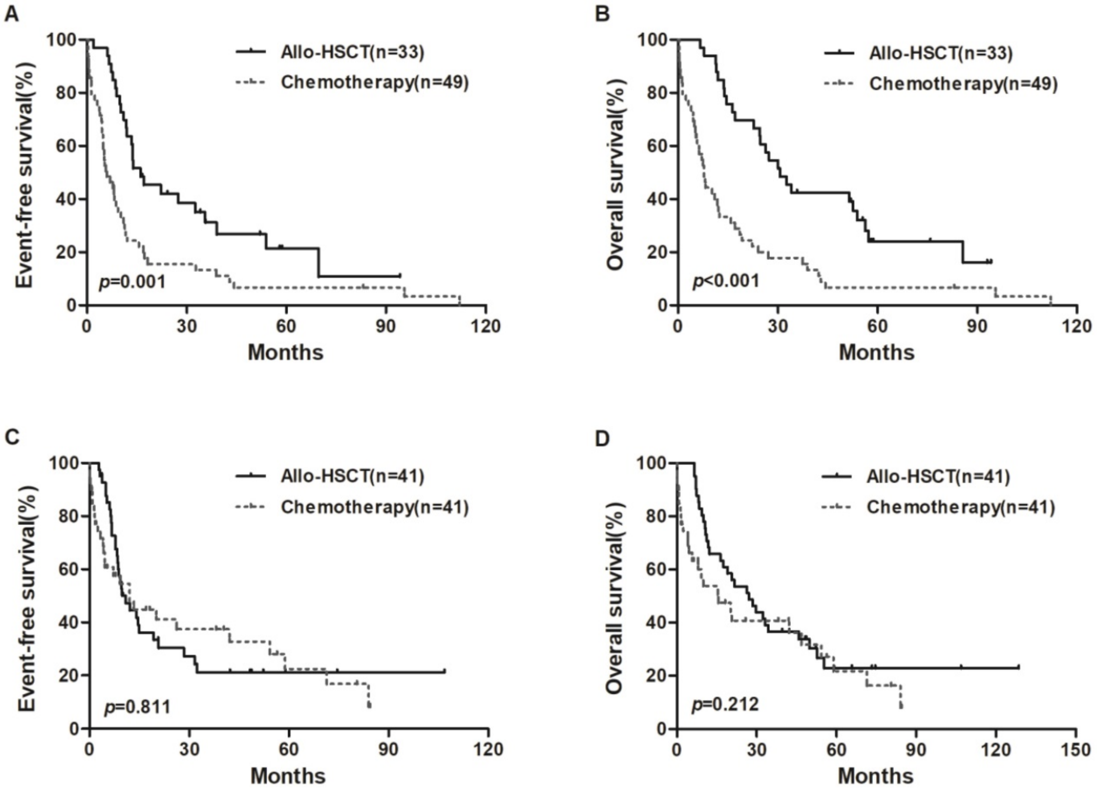

Figure 2. Kaplan-Meier curves of EFS and OS in high and low miR-98 expression groups. (A, B) In low expression group, patients treated with allo-HSCT had longer EFS and OS than those treated with chemotherapy-only. (C, D) No significant survival differences were found between chemotherapy group and allo-HSCT group in high miR-98 expressors.

significantly associated with miR-98 expression ($P < 0.05$, fold change = 1.5, Figure 3A). Second, we identified 277 genes were positively correlated with miR-98 expression, and 256 genes were negatively correlated with miR-98 expression ($P < 0.05$, fold change = 1.5, Figure 3B). These genes were presented in the aberrant expression heat map (Figure 3C). Further gene ontology (GO) enrichment analysis indicated that the genes associated with miR-98 expression were mainly involved in "embryonic skeletal system morphogenesis", "definitive hemopoiesis", "thyroid gland development", "negative regulation of myeloid cell differentiation", "L1CAM interactions", "signaling pathways regulating pluripotency of stem cells", "drug catabolic process", "sensory perception of sound", and "response to inorganic substance" pathways. (Figure 3D).

Discussion

Our study found that high miR-98 expression was more likely to occur in younger and good-risk patients, and more *RUNX1-RUNX1T* fusion was seen in high miR-98 expression group, suggesting that high miR-98 expression tend to coincide with good-risk AML and may have similar prognostic value as *RUNX1-RUNX1T*.

In the chemotherapy group, multivariate analysis had proved that low miR-98 expression and age ≥ 60 were independent adverse factors. But in the allo-HSCT group, univariate and multivariate analysis all showed no effect of miR-98 expression on EFS and OS, and in the entire cohort, the low miR-98 expressors who underwent allo-HSCT had longer EFS and OS. In all patients, multivariate analysis indicated that allo-HSCT was independent favorable factor for both EFS and OS. Thus, we speculated that the unfavorable influence of low miR-98 expression might be overcome by allo-HSCT.

The mechanisms of miR-98 in anti-tumorigenesis have been investigated. MiR-98 could suppress breast cancer angiogenesis and invasion by repressing the expression of *ALK4* and *MMP11* [25]. MiR-98 could also suppress the growth and metastasis of salivary adenoid cystic carcinomas by inhibiting the oncogene *NRAS* via the regulation of the *RAS/MAPK/ERK* and *PI3K/AKT* pathways [26] and suppress cell invasion and migration in glioma by directly targeting Pre-B Cell Leukemia Homeobox 3 [27]. It targeted *SALL4* to inhibit proliferation, migration, and invasion of hepatocellular carcinoma [28]. It inhibited melanoma metastasis via inhibiting IL-6 signaling pathway [22]. Mir-98 could negative regulate the expression of tumor suppressor gene FUS1b in lung cancers [29]. In

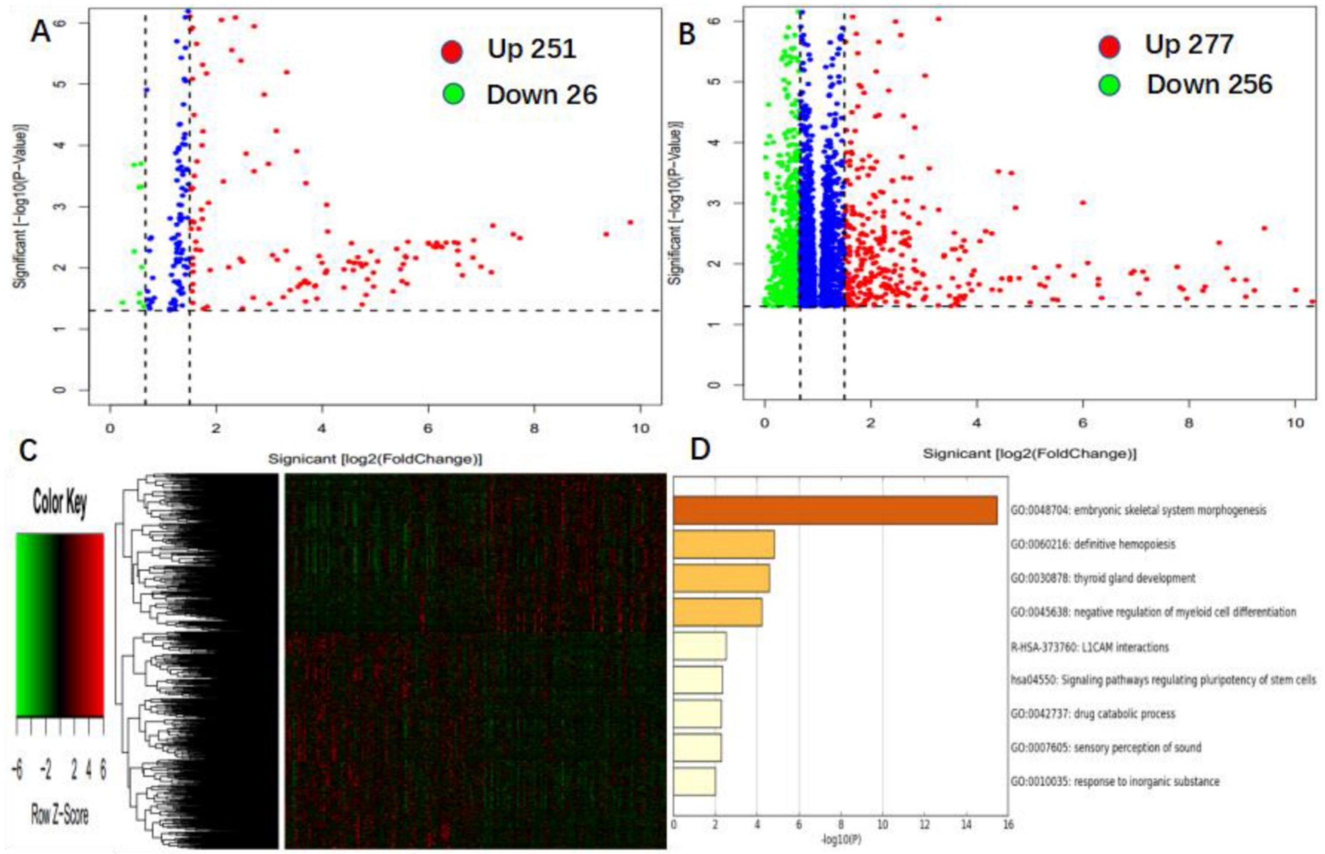

Figure 3. Genome-wide gene/microRNA expression profile and cell signaling pathways associated with miR-98 expression. (A) Volcano plot of differential microRNA expression. miR-98^{high} and miR-98^{low} were marked by red and green circles, respectively. (B) Volcano plot of differential gene expression. miR-98^{high} and miR-98^{low} were marked by red and green circles, respectively. (C) Expression heatmap of associated with miR-98 expression. (D) Gene ontology (GO) enrichment analysis of genes related to miR-98 expression.

leukemia, it was found that miR-98 upregulation could improve chemotherapy-sensitivity and decrease leukemia cell proliferation by inhibiting *E2F1* expression [30]. In the present study, miR-98 is associated with "definitive hemopoiesis", "negative regulation of myeloid cell differentiation", "signaling pathways regulating pluripotency of stem cells", and they play an important role in hematopoiesis, which suggests that miR-98 may play a prognostic role in leukemia by interacting with genes involved in these functional pathways. The detailed mechanism of miR-98 in AML leukemogenesis, however, should require further study.

In summary, we found that high miR-98 expression was a good prognostic factor in AML patients who only received chemotherapy. Patients with low miR-98 expression may benefit from allo-HSCT.

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Competing Interests

The authors have declared that no competing interest exists.

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