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GATA2 mutations and overexpression in pediatric acute myeloid leukemia

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ABSTRACT

Background: *GATA2* is important for the regulation of development and proliferation of early pluripotent hematopoietic precursors, and precise *GATA2* expression is critical in myeloid lineage maturation. *GATA2* mutations have been reported in acute myeloid leukemia (AML) but only few studies of *GATA2* mutations and overexpression in pediatric AML have been reported so far and none was in Chinese populations.
Method: We analyzed *GATA* mutation status and expression state in a cohort of 309 Chinese children with AML. We also assessed the impact of *GATA2* mutations and overexpression on outcomes in our pediatric AML cohort.
Results: *GATA2* mutations were observed in 2.6% of the patients and they were clustered in the ZF1 and ZF2 domains. *GATA2* overexpression was detected in 72.7% of the cases, with the highest and lowest expression levels observed in adverse subgroup and favorable subgroup, respectively. In the entire cohort, shorter overall survival (OS) and event-free survival (EFS) showed a stronger correlation with *GATA2* overexpression than with normal *GATA2* levels (OS: $p = 0.021$; EFS: $p = 0.018$). Such an inverse relationship between *GATA2* overexpression and survivals was evident among AML patients with normal cytogenetics (OS: $p = 0.037$; EFS: $p = 0.024$) and adverse features (OS: $p = 0.021$; EFS: $p = 0.023$), but not observed in favorable subgroup (OS: $p = 0.323$; EFS: $p = 0.342$), suggesting that the negative influence of *GATA2* overexpression on pediatric AML outcomes is risk subgroup specific.
Conclusion: Our results demonstrate that *GATA2* mutations in pediatric AML are rare, and are primarily clustered in the zinc finger (ZF) domains. Our results suggest that *GATA2* overexpression exerts a negative influence on survivals, and the effect is risk subgroup specific in pediatric childhood AML.

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1. Introduction

Acute myeloid leukemia (AML) is a group of heterogeneous diseases with differences in clinical and genetic features [1–3]. Although considerable progress has been made in AML treatment in the past decade [4,5], more than 50% of AML patients relapse and do not survive beyond 5 years, underlining the importance of identification of new biomarkers to inform risk stratification to develop risk-adapted treatment of AML [3,6].

The GATA-binding protein 2 (*GATA2*) gene on chromosome 3q21.3 encodes a zinc-finger transcription factor that functions as a tissue-specific master transcriptional regulator [7]. The primary role of *GATA2* is to regulate the development and proliferation of early pluripotent hematopoietic precursors [8,9]. Germline *GATA2* mutations are responsible for GATA2 deficiency syndrome that is characterized by hematologic, infectious, and pulmonary manifestations [10], whereas acquired somatic *GATA2* mutations are present in hematologic malignancies, primarily in erythroid and myeloid lineages including myelodysplastic syndrome and AML, and occasionally in lymphoid disorders as well [11–14]. Tight *GATA2* expression is critical in myeloid lineage maturation [15], and aberrant *GATA2* expression has been described in AML [16]. Although early studies indicate *GATA2* overexpression as a poor prognostic indicator in pediatric AML, its impact on different AML risk subgroups needs further studies [17–20]. Thus far, there have been only few reports on *GATA2* mutations and expression in childhood AML, and most of the reported studies were on populations in the West [13,17].

It is now recognized that pediatric and adult AML represent two genetically distinct diseases, and even the same genetic aberrations may exert differently on outcomes in two age groups [21,22]. Moreover, difference in AML genetic mutational profiles and clinical significance between ethnic and race groups are well documented [23–25]. Thus far, the majority of data on *GATA2* mutational profiling and prognostic significance of *GATA2* overexpression in AML are derived from studies on adults in the Western populations and none was in Chinese children with AML [17,18,26–28].

Our study is aimed to investigate the molecular characteristics and clinical relevance of *GATA2* mutations and expression in a large cohort of *de novo* childhood AML in a Chinese population. Our results demonstrate that *GATA2* mutations in childhood AML are rare, and they are primarily clustered in the zinc finger (ZF) domains. We study revealed that *GATA2* overexpression exerted a negative influence on survival, and such an effect was evident in normal cytogenetics subgroup and adverse subgroup but not in favorable AML subgroup, suggesting that *GATA2* overexpression is a risk subgroup-specific prognostic indicator in childhood AML. Results from our study underpin and extend earlier findings of *GATA2* mutations and expression in pediatric AML.

2. Patients and methods

2.1. Patients

A total of 345 patients with new AML were enrolled between 2007 and 2018 at the Children's Hospital of Chongqing Medical University in China. Diagnosis of AML was made based on histology, genetics, and immunology studies. None of the patients in our cohort had clinical features of Emberger syndrome, immunodeficiency, aplastic anemia or myelodysplastic syndrome prior to diagnosis of AML. The patients received a daunorubicin/cytarabine/etoposide (DAE)-based regimen according to following the Protocols of the Pediatric Hematology Group of Chinese Medical Association [29]. This study was reviewed and approved by the Ethics Committee of the Children's Hospital of Chongqing Medical University in accordance with the Declaration of Helsinki.

2.2. Cytogenetics analysis and risk subgroup classification

Karyotyping analysis and fluorescence *in situ* hybridization (FISH) were performed following standard procedures. Prognostic risk subgroups were determined according to the international expert panel recommendation based on major cytogenetic and molecular genetics features: AML bearing core binding factor (*CBF*) rearrangements, *NPM1* mutations or *CEBPA* bi-allelic mutations (normal karyotype) as a favorable subgroup, those with *FTL3*-internal tandem duplication (ITD), complex cytogenetics and monosomy 5 or 7 etc. being assigned as adverse subgroup, and the rest of the cases as intermediate subgroup [22].

2.3. Gene mutation analysis

Of the 345 cases enrolled in the study, *GATA2* mutation analysis was completed in 309 cases. DNA was extracted from the diagnostic bone marrow using the TIANamp Blood DNA kit (Tiangen Biotech, Beijing, China). DNA segment covering the exon 4 of *GATA2* was amplified by Touch Down polymerase chain reaction (PCR) using the primers-5′GGGAGACC CTCTCGTCCCTCTTCCTGCCCAGGC3′ and 5′GGCCCCCAAAGCAG GGAACGATTTAA GCCTCATA3'. The PCR protocol as follow: one cycle of 94 °C, 4 min; 8 cycles of 94 °C, 30 s; 72°C–65 °C, 30 s, and 68°C–64 °C, 45 s; 32 cycles of 94 °C, 30 s; 65 °C, 30 s, and 68 °C, 45 s, and a final extension at 68 °C, 5 min. DNA segment containing *GATA2* exons 5 and 6 was amplified by step-down PCR with one cycle of 94 °C, 2 min; 5 cycles of 98 °C, 10 s, 74 °C, 80 s; 5 cycles of 98 °C, 10 s, 72 °C, 80 s; 5 cycles of 98 °C, 10 s, 70 °C, 80 s; 20 cycles of 98 °C, 10 s, 68 °C, 80 s, and a final extension at 68 °C, 7 min. The primers 5′AGGGGGACCAAGCCGGCTCAGC CTCAGGAT3′ and 5′GCTGGGCCGAGCCGGGCTGGC3′ were used for PCR amplification of exons 5 and 6. The PCR products were analyzed by Sanger sequencing. Germline *GATA2* mutation status was examined by analysis of DNA extracted from buccal swab or remission bone marrow specimens of the patents with mutant *GATA2*. Mutations in *FLT3*/ITD (exons 14–15), *NPM1* (exon 12), *WT1* (exons 7 and 9), *N-RAS* (exons 1–2), *K-RAS* (exons 1–2), *IDH1* (exon 4), *KIT* (exons 8, 10, 11 and 17), *CEBPA* (exon 1), *CCDN1* (exon 5), *CCDN2* (exon 5), *ASXL2* (exons 11 and 12), and *DHX15* (exon 3) were examined according to the previously described methods [30–41]. PolyPhen and SIFT programs were employed to predict the effect of the variants on the structure and function of *GATA2* protein [42,43].

2.4. GATA2 expression analysis

In 150 cases, for which RNA samples were available, *GATA2* expression level was assessed. Total RNA was isolated from diagnostic bone marrow using the TRIzol Reagent (Thermo Fisher Scientific, Waltham, MA). Reverse transcription was performed using the PrimeScript TM RT Reagent Kit and gDNA Eraser (Takara Bio, Inc. Shiga, Japan). *GATA2* mRNA levels were determined using the SYBR Green Real-Time PCR Master Mixes (Thermo Fisher Scientific, Waltham, MA) with ABI 7500 Fast Real-Time PCR System (Applied Biosystems, Foster City, CA). 5′CATCAAGCCCAAGCGAAGACT3′ and 5′CAGCTCCTCGA AGCACTCCG3′ were used as primers. *GADPH* served as an endogenous control with primers 5′CAGGGCTGCTT TTAACTCTGG3′ and 5′GGGTGGAATCATATTGGAACA3′. Bone marrow from 41 individuals with no evidence of hematological neoplasm was used as controls. The following PCR protocol was used: one cycle of 95 °C, 10 min; 40 cycles of 95 °C, 15 s; 60 °C, 60 s. Each sample was run in triplicate. *GATA2* transcript relative quantification values were calculated by the $2^{-\triangle\triangle ct}$ method [44]. *GATA2*

was considered to be overexpressed if it showed expression greater than the control median plus 3 standard deviations [18].

2.5. Statistical analysis

Variables were compared using chi-square (χ^2) test. In cases for which expected values from contingency tables were smaller than 5, the Fisher's exact was applied. The Mann-Whitney test was used to determine the significance between differences in medians. Overall survival (OS) was defined between the date of diagnosis and date of death from any cause or last contact. Event-free survival (EFS) was the time between diagnosis and occurrence of the first event such as no complete remission as event on day 0, relapse, secondary tumor or death. OS and EFS were calculated using the Kaplan-Meier analysis, and the differences were compared by using log-rank test. A p value of $\leq$0.05 (two-sided) was considered statistically significant. All statistically analyses were performed using SPSS software package v17.0 (SPSS, Inc., Chicago, IL).

3. Results

3.1. GATA2 mutations

Of 309 cases with material available for analysis, distinct *GATA2* variants were identified in eight patients, resulting in a *GATA2* variant frequency of approximately 2.6%. Buccal DNA or marrow at remission was available to confirm that the GATA2 mutations detected in this study were not germline variants. Four of the *GATA2* variants were in exon 6, three in exon 5, and one in exon 4. Four variants were in the zinc-finger (ZF) domains: three in the ZF1 domain (cases 2, 5 and 7), and one in the ZF2 domain (case 6), and the other four variants were within the C-terminus region distal to the ZF domains. Five variants were deemed pathogenic whereas three (cases #3, #4 and #8) were benign changes using the PolyPhen and SIFT programs. One mutant *GATA2* case showed elevated *GATA2* expression. The t(8;21)(q22;q22) was present in three (37.5%) cases, monosomy 7 in two (25%), and t(15;17) in one (12.5%). Five (62.5%) cases belonged to the favorable prognostic subgroup and three were assigned to adverse subgroup. Of seven patients with outcome information available, two failed to reach remission and died within one month. Among the five patients who achieved remission, two relapsed and died within one month and 14 months, respectively, and the other three were alive in 6, 25 or 57 months in the last contact (Table 1). None of the patients with mutant *GATA2* had a history of bone marrow transplant.

3.2. GATA2 expression in pediatric AML

Among the 150 cases with RNA samples available for *GATA2* expression analysis, 109 (72.7%) patients showed elevated *GATA2* transcripts. The median *GATA2* expression levels in the whole cohort and risk subgroups were all significantly higher than the normal controls ($p < 0.001$). No significant difference in clinical or molecular features was present between the high and normal level expression groups, except a higher frequency of *KIT* mutations among the patients with high *GATA2* overexpression (Table 2). Among the AML risk subgroups, adverse subgroup had the highest median *GATA2* expression level followed by normal cytogenetics (CN) AML, intermediate, and favorable subgroups with the difference between the adverse and favorable subgroups reaching statistical significance ($p = 0.02$) (Fig. 1).

3.3. Influence of GATA2 overexpression on pediatric AML outcomes

Follow-up information was available from 106 patients whose

Table 1
Clinical and molecular characteristics of mutant *GATA2* cases.

Case No.	Exon	Mutation	Age (years)/ sex	WBC count ($x10^9$/L)	*GATA2* overexpression	Other gene mutation	Karyotype	Outcome			
								Remission	Relapse	Overall survial (months)	Last contact
1	6	c.1260C > A/p.C420*	9/M	11.14	yes	*WT1*	46,XY,t(15;17)(q22;q11.2) [16]/46,XY [4]	yes	yes	14	died
2	4	c.920G > T/p.R307L	5/M	255.47	no	*CEBPA* (biallelic)	46,XY [20]	no	n/a	1	died
3	6	c.1198A > T/p.M400L	7/F	13.14	no	n.d.	46,XX,t(8;21)(q22;q22),del(9)(q22q32) [15]/46,XX [5]	n/a	n/a	n/a	lost contact
4	6	c.1231G > T/p.A411S	2/M	9.53	no	n.d.	50,XY,add(3)(q12),+6,t(6;12)(p25;p13),+13,+19,+21,+mar [20]	no	n/a	1	died
5	5	c.1109G > T/p.C370F	5/F	6.23	no	n.d.	45,X,-X,t(8;21) (q22;q22) [19]/46,XX [1]	yes	no	57	alive
6	5	c.1095C > G/p.N365K	1/M	38.45	no	n.d.	45,XY,-7 [20]	yes	no	25	alive
7	5	c.1018-1028delTCGGCCGCCAG/ p.S340fs*40	8/F	84.06	no	n.d.	45,XY,-7 [20]	yes	yes	4	died
8	6	c.1237T > A/p.C413S	14/F	4.63	no	n.d.	46,XX,t(8;21)(q22;q22),del(9)(q22) [2]/46,XX [1]	yes	no	6	alive

Note: n/a: not applied; Refseq for GATA2: NM_001145661.1.

Table 2
Clinical and molecular features of patients with normal expression or overexpression of *GATA2*.

	Overexpression (n = 109)	Normal (n = 41)	*p*
Age, y (n = 150)			
median (range)	6 (0.24–16)	8 (0.42–14)	n.s.
range			
distribution			
<3	31 (28.4)	8 (19.5)	n.s.
3 ≤ and <10	51 (46.8)	19 (46.3)	
≥ 10	27 (24.8)	14 (34.1)	
Male (%) (n = 85)	66 (60.6)	19 (46.3)	n.s.
WBC, $x10^9$/L, median (range) (n = 150)	19.75 (0.21–360.99)	11.16 (1.0–292.4)	n.s.
Hemoglobin, g/L, median (range) (n = 150)	75 (26–140)	73.0 (40–103)	n.s.
Platelet, $x10^9$/L, median (range) (n = 150)	38.0 (3–558)	38.0 (6–309)	n.s.
Bone marrow blasts (%), median (range) (n = 150)	70.0 (3.5–99)	72.0 (16.5–95)	n.s.
Risk subgroups, n (%) (n = 125)			
adverse	16 (17.8)	4 (11.3)	n.s.
intermediate	41 (45.6)	14 (40.0)	
favorable	33 (36.7)	17 (48.6)	
Mutant			
WT1 (n = 140)	9/101 (8.9)	2/39 (5.1)	n.s.
FLT3/ITD (n = 141)	9/101 (8.9)	1/40 (2.5)	n.s.
KIT (n = 136)	5/96 (5.2)	8/40 (20.0)	0.02
IDH1 (n = 141)	2/101 (2.0)	0/40 (0)	n.s.
N-RAS/K-RAS (n = 142)	12/102 (11.8)	3/40 (7.5)	n.s.
CEBPA (n = 140)	12/100 (12.0)	3/40 (7.5)	n.s.
NPM1 (n = 134)	4/101 (4.0)	1/40 (2.5)	n/a
CCND1 (n = 114)	0/85 (0)	0/29 (0)	n/a
CCND2 (n = 113)	0/82 (0)	0/31 (0)	n/a
GATA2 (n = 130)	1/93 (1.1)	0/37 (0)	1.00
ASXL2 (n = 124)	0/95 (0)	0/29 (0)	n/a
DHX15 (n = 100)	0/85 (0)	0/15 (0)	n/a
Outcome (n = 101)			
Relapse	31/70 (44.3)	9/36 (25.0)	0.05
Complete remission	41/70 (58.6)	29/36 (80.6)	0.02

Note: n.s.: not significant; n/a: not applied.

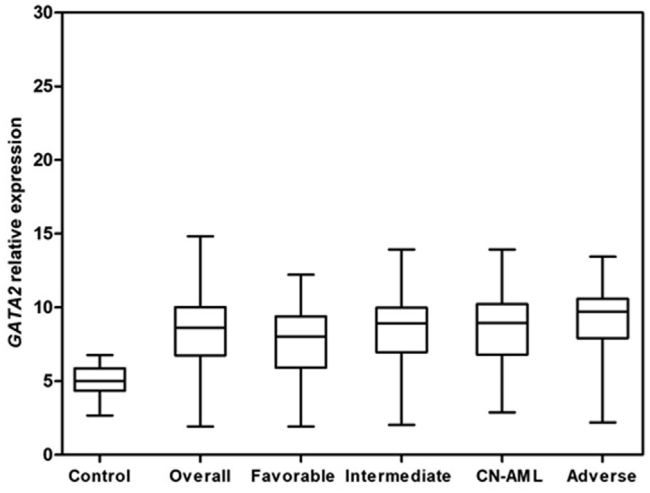

Fig. 1. Normalized *GATA2* expression levels in the whole cohort and AML risk subgroups. Box plots showing interquartile distributions (25%–75%), medians (horizontal line within boxes), and range distribution (97%; represented by whiskers).

GATA2 expression levels were assessed. Compared with those with non-elevated expression, the patients with *GATA2* overexpression had a lower complete remission rate and higher relapse rate. The differences in complete remission rate and relapse rate were prominent in CN-AML and adverse-risk subgroups, and a similar trend was noted in the intermediate risk AML, but not in favorable risk subgroup (Table 3). Kaplan-Meier analysis of the whole AML cohort demonstrated that elevated *GATA2* expression was associated with shorter OS ($p = 0.021$) and EFS ($p = 0.018$). Such an inverse correlation between *GATA2* overexpression and survivals was retained in the CN-AML subgroup (OS: $p = 0.037$; EFS: $p = 0.024$) and marginal significance was observed in the intermediate subgroup (OS: $p = 0.108$; EFS: $p = 0.142$). Although the number of patients in the adverse subgroup was small, the results also demonstrate shorter survivals for children with high *GATA2* expression compared with normal expression (OS: $p = 0.029$; EFS: $p = 0.030$). No difference in survival was observed in the favorable risk subgroup (OS: $p = 0.323$; EFS: $p = 0.346$) (Figs. 2–3).

Table 3
Comparison of outcomes of *GATA2* overexpression and normal expression in AML risk subgroups.

	Overexpression, n (%)	Normal, n (%)	*p*
Favorable (n = 43)	27	16	
Relapse	7 (25.9)	3 (18.8)	n.s.
Complete remission	19 (70.4)	13 (81.3)	n.s.
Intermediate (n = 39)	27	12	
Relapse	14 (51.9)	4 (33.3)	n.s.
Complete remission	15 (55.6)	10 (83.3)	n.s.
CN-AML (n = 21)	15	6	
Relapse	8 (53.3)	0	0.046
Complete remission	10 (66.6)	6 (100)	n.s.
Adverse (n = 13)	9	4	
Relapse	7 (77.7)	0	0.021
Complete remission	4 (44.4)	4 (100)	n.s.

Note: n.s.: not significant.

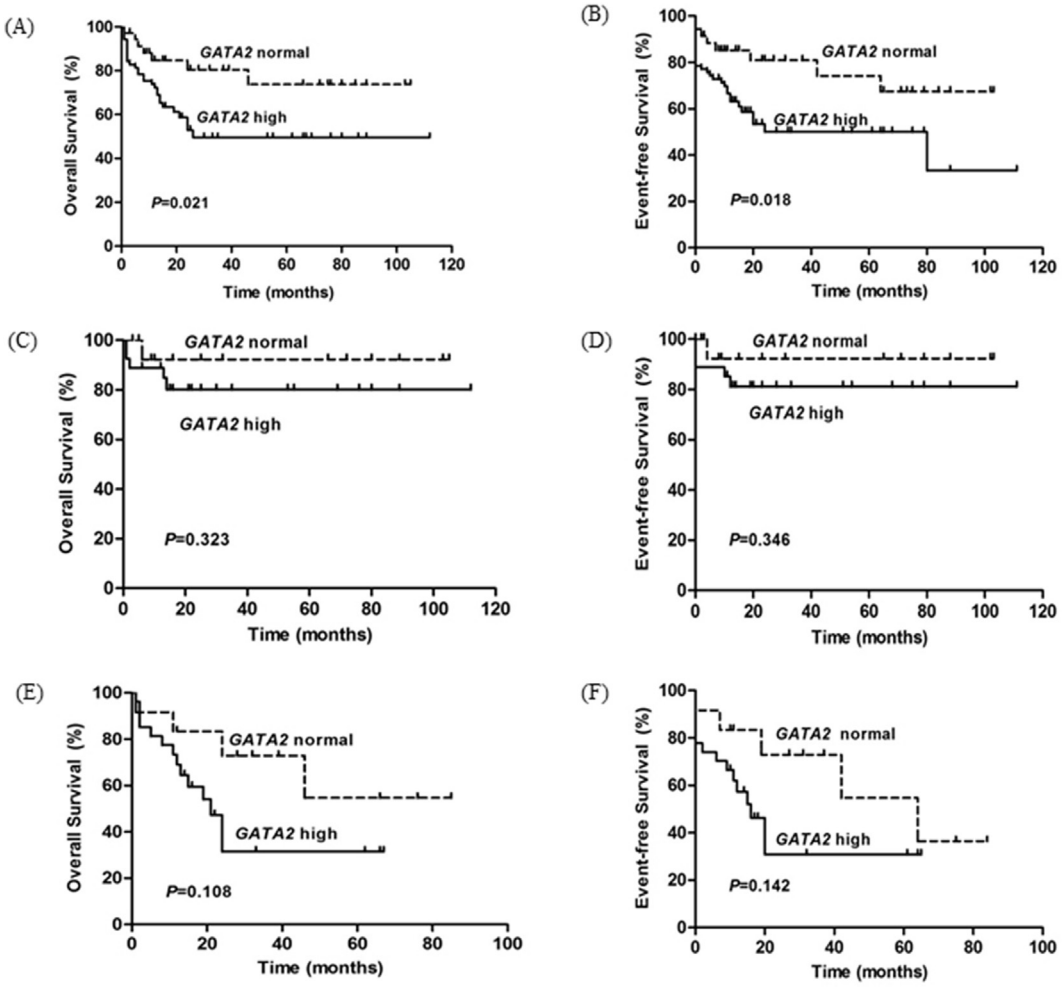

Fig. 2. Kaplan-Meier plots of OS and EFS for AML with *GATA2* overexpression and normal expression. (A–B) OS and EFS curves of whole cohort with overexpression and normal expression of *GATA2* (OS: $p = 0.021$, EFS: $p = 0.018$); (C–D) OS and EFS curves of favorable AML subgroup with overexpression and normal expression of *GATA2* (OS: $p = 0.323$, EFS: $p = 0.346$); (E–F) OS and EFS curves of intermediate subgroup with overexpression and normal expression of *GATA2* (OS: $p = 0.108$, EFS: $p = 0.142$).

4. Discussion

It is now well recognized that differences in genetic landscape of AML exist not only between children and adults [21,45], but also between racial and ethnic groups as well [23–25]. For instance, core-binding factor (CBF) leukemia associated with *CBFB-MYH11* fusion or *RUNX1-RUNX1T1* is much higher in Eastern Asia than in Europe and North America, while *MPN1*, *FLT3*-ITD and *DNMT3A* mutation frequencies are higher in Caucasians than in Chinese and Japanese [25,46–48]. The results from a study of the US Children's Oncology Group demonstrate a racial difference in the impact of *TET2* SNP rs245206 on pediatric AML outcomes [24]. So far, no studies of *GATA2* mutations and expression in pediatric AML in Chinese populations have been reported in the literature.

GATA2 is a zinc finger transcription factor important for hematopoietic stem cell proliferation and normal megakaryocytic development [8,9,15]. *GATA2* mutations are rare in AML and myelodysplastic syndrome (MDS) with reported incidence of 2%–5.5%, but are common in adult acute erythroid leukemia (22.4%) in the West [17,49]. The prevalence of *GATA2* mutations observed in our childhood AML cohort (2.6%) is in agreement with the ones from other AML studies. The occurrence of higher incidences of *GATA2* mutations in CN-AML has been reported in childhood AML [17]. However, we observed no difference in *GATA2* mutation frequency between AML overall and CN-AML cohorts (2.6% vs. 2.0%). Half of the *GATA2* variants in our cohort were located in the ZF domains compared to most of the mutations reported from other studies [12,28,50]. The ZF domains of *GATA2* contribute to the stabilization of its structure and specificity of DNA binding, and mediate its interaction with the transcriptional factor Friend of GATA1 (FOG1), whereas its C-terminus interacts with *CEBPA* [13,51].

Co-occurrence of *GATA2* and biallelic *CEBPA* mutations has been described in adult AML, as both genes are involved in the same differentiation pathway, which when altered results in leukemogenesis [28,52]. However, Shiba and colleagues observed no such concomitant mutations in childhood AML [13]. In the present study reported here, co-existence of *GATA2* and bi-allelic *CEBPA* mutation was found in one patient. Furthermore, Shiba et al. reported that mutant *GATA2* is more likely to be found in pediatric AML with either favorable or intermediate cytogenetics features [13]. In their study of European children and adolescents with myelodysplastic syndrome (MDS), Wlodarski and colleagues observed a very high prevalence of germline *GATA2* mutation in adolescent MDS bearing monosomy 7 (72%), and *GATA2* mutational status had no effect on survivals [53]. Of the eight patients with *GATA2* mutations in our cohort, four had favorable cytogenetics features [t(15;17) and t(8;21)], two had monosomy 7, one normal cytogenetics, and one complex abnormalities. The two patients with monosomy 7 were

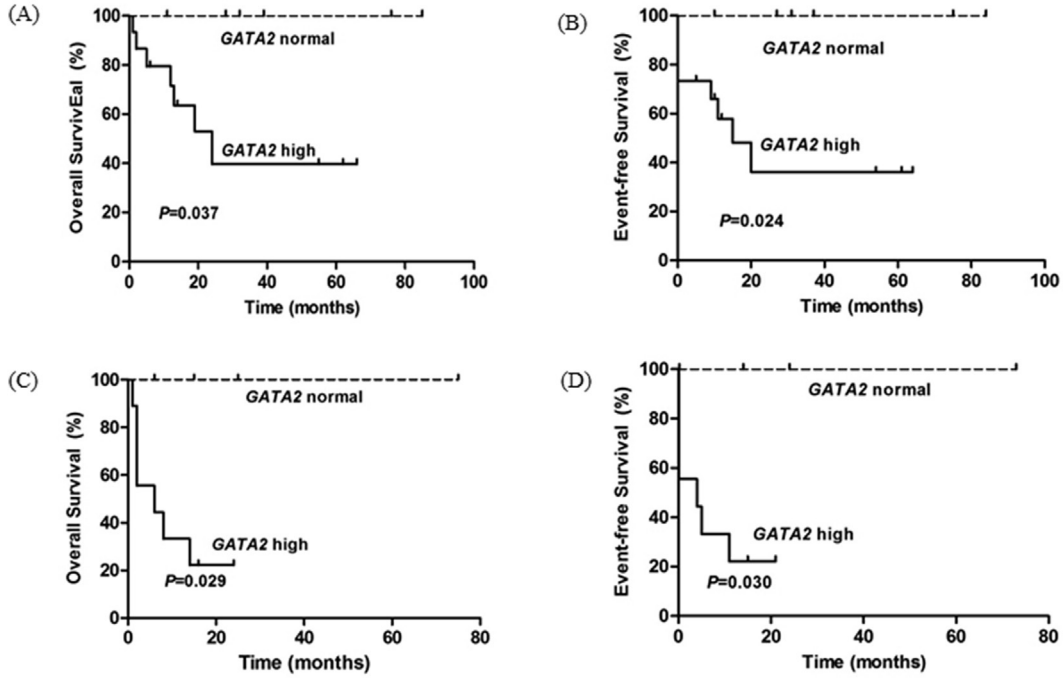

Fig. 3. Kaplan-Meier plots of OS and EFS for AML with *GATA2* overexpression and normal expression; (A–B) OS and EFS curves of CN-AML with overexpression and normal expression of *GATA2* (OS: $p = 0.037$, EFS: $p = 0.024$);(C–D) OS and EFS curves of adverse subgroup with overexpression and normal expression of *GATA2* (OS: $p = 0.029$, EFS: $p = 0.030$).

young at diagnosis: one and eight year-old, and the monosomy 7 prevalence in our mutant *GATA2* AML subset (25%) is comparable with whole pediatric AML [21].

The prognostic significance of *GATA2* mutations in AML still remains elusive. Some have reported that AML with *GATA2* mutations may have improved outcomes [13,26] while others failed to demonstrate negative effect of *GATA2* mutations on AML outcomes [28]. These are largely attributed to low GATA2 mutation prevalence in AML and much lower AML incidence in children than in adults. In our cohort, half of the patients with *GATA2* mutation did not survive beyond 1.5 years, indicating negative effect of *GATA2* mutations on outcomes in pediatric AML. Our results should be validated by large studies in the future.

Hematopoietic stem cells are sensitive to *GATA2* expression [8,54], and tightly balanced *GATA2* expression is critical for their proliferation and maintenance [55,56]. *GATA2* is highly expressed in immature hematopoietic cells and down regulated during lineage commitment [57–59]. It has been suggested that elevated levels of *GATA2* may lead to the interaction of GATA2 with *N-MYC* and *HOXA9*, resulting in self-renewal and proliferation of myeloid progenitors, contributing to leukemogenesis [60,61]. There have been limited reports on the study of *GATA2* expression in AML and fewer in childhood AML [17–20]. The *GATA2* overexpression prevalence observed in our study is in line with the observations reported in childhood AML (65%) and adult AML study (87%) [17,20]. The study of Vicente et al. shows inferior survivals of adult AML with elevated *GATA2* expression in a Spain population [18] and Luesink and colleagues demonstrate high *GATA2* expression as a poor prognostic indicator in pediatric AML, particularly in CN-AML [17]. We also observed negative impact of high *GATA2* expression on outcomes (higher relapse rate, lower complete remission rate, and shorter survivals) in our pediatric AML cohort. Further analysis of the influence of *GATA2* expression on outcomes among AML subgroups in our cohort shows the difference was retained in the CN-AML and adverse AML subgroups and a similar trend was also observed in the intermediate risk subgroup, but not in the favorable subgroup, indicating that the effect of *GATA2* overexpression on childhood AML may be prognostic subgroup-specific. Future investigations of larger cohorts are needed to confirm our observations.

The discrepancies between our findings and other studies may be attributed to difference in genetic profile between adult and childhood AML, racial and ethnic groups, AML subtypes included in the study, and methodologies employed in *GATA2* expression analysis [13,17,18,20,26–28,62].

In conclusion, we report a study of *GATA2* mutational profile and expression in a large cohort of pediatric AML in a Chinese population. *GATA2* mutations were present in 2.6% of the cases while overexpression prevalence was 72.7% with the highest in adverse risk subgroup and lowest in favorable subgroup. *GATA2* overexpression was correlated with shorter survivals, and the negative effect of *GATA2* overexpression on outcome was retained in AML with normal cytogenetics and adverse-risk subgroups but not in favorable subgroup, suggesting that the negative influence of *GATA2* overexpression on pediatric AML prognosis is risk subgroup-specific. Our study underpins and extends earlier findings of *GATA2* mutation and expression in childhood AML.

Conflicts of interest

The authors declare no conflicts of interest.

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