RESEARCH ARTICLE

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The *lnc-SNHG1* Gene Is Overexpressed and Correlates with Increased White Blood Cell Count, Poor Induction Treatment Response, and Poor Survival Profile in Adult Acute Myeloid Leukemia

Yetişkin Akut Myeloid Lösemide *lnc-SNHG1* Geni Aşırı İfade Edilir ve Artan Beyaz Kan Hücresi Sayısı, Zayıf İndüksiyon Tedavi Yanıtı ve Kötü Sağkalım Profili ile İlişkilidir

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Abstract

Objective: *Long noncoding RNA small nucleolar RNA host gene 1* (*lnc-SNHG1*) is involved in leukemogenesis via mediating multiple pathways. The current study aimed to further explore its clinical roles in disease risk, clinical features, and prognosis in patients with acute myeloid leukemia (AML).

Materials and Methods: A total of 161 adult AML patients, 50 patients as a disease control (DC) group, and 50 healthy individuals as a healthy control (HC) group were enrolled and bone marrow mononuclear cells were collected. Subsequently, reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed to measure *lnc-SNHG1* expression.

Results: *Lnc-SNHG1* expression was higher in AML patients than in the DC and HC groups (both p<0.001), with good value in distinguishing AML patients from DC and HC individuals (area under the curve of 0.726 and 0.884, respectively). Moreover, *lnc-SNHG1* expression was positively associated with white blood cell (WBC) count (p=0.008) but was not correlated with other clinical features such as cytogenetics, molecular genetics, and risk stratification (all p>0.05). *Lnc-SNHG1* expression was also associated with a lower complete remission (CR) rate (p=0.001). Patients with *lnc-SNHG1* expression in the fourth quantile had the worst CR rates compared to patients with *lnc-SNHG1* expressions in the first, second, and third quantiles (all p<0.05). Furthermore, *lnc-SNHG1* expression was correlated with unsatisfactory event-free survival (p<0.001) and overall survival (p=0.002), which were worst in patients with *lnc-SNHG1* expression in the fourth quantile compared to patients with *lnc-SNHG1* expressions in the first, second, and third quantiles (all p<0.05).

Öz

Amaç: *Uzun kodlamayan RNA küçük nükleolar RNA konak gen 1 (lnc-SNHG1),* çoklu yolaklara aracılık ederek lökomogenezde yer alır. Mevcut çalışma, akut myeloid lösemili (AML) hastalarda bu genin hastalık riski, klinik özellikler ve prognozdaki klinik rolünü daha ayrıntılı araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Toplam 161 yetişkin AML hastası ile birlikte, 50 hasta hastalıklı kontrol grubu (HK) olarak, 50 sağlıklı birey sağlıklı kontrol (SK) grubu olarak çalışmaya alındı ve kemik iliği mononükleer hücreleri toplandı. Ardından, *lnc-SNHG1* ifadesini ölçmek için ters transkripsiyon-kantitatif polimeraz zincir reaksiyonu (RT-qPCR) yapıldı.

Bulgular: *Lnc-SNHG1* ifadesi AML hastalarında HK ve SK gruplarına göre daha yüksekti (her ikisi de p<0,001) ve AML hastalarını HK ve SK bireylerden ayırt etmede iyi bir değere sahipti (sırasıyla eğrinin altındaki alan 0,726 ve 0,884). Ayrıca, *lnc-SNHG1* ifadesi, beyaz kan hücresi (WBC) sayısı ile pozitif olarak ilişkiliydi (p=0,008) ancak sitogenetik, moleküler genetik ve risk sınıflandırması gibi diğer klinik özelliklerle korele değildi (tümü p>0,05). *Lnc-SNHG1* ifadesi ayrıca daha düşük bir tam remisyon (TR) oranı ile ilişkilendirilmiştir (p=0,001). Dördüncü çeyrekte lnc-SNHG1 ekspresyonu olan hastalar, birinci, ikinci ve üçüncü çeyrekte *lnc-SNHG1* ifadesi olan hastalara kıyasla en kötü TR oranlarına sahipti (tümü p<0,05). Ayrıca, lnc-SNHG1 ekspresyonu, olaysız sağkalım (p<0,001) ve genel sağkalım (p=0,002) oranlarında tatmin edici olmayan sonuçlarla ilişkili bulundu.

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Abstract

Conclusion: *Lnc-SNHG1* overexpression is associated with elevated WBC count, poor induction treatment response, and poor survival profile in cases of AML and it may serve as a potential indicator for AML.

Keywords: Acute myeloid leukemia, *Long noncoding RNA small nucleolar RNA host gene 1*, Complete remission, Event-free survival, Overall survival

Öz

Sonuç: *Lnc-SNHG1* aşırı ekspresyonu, AML olgularında yüksek WBC sayısı, zayıf indüksiyon tedavisi yanıtı ve kötü sağkalım profili ile ilişkilidir ve AML için potansiyel bir gösterge görevi görebilir.

Anahtar Sözcükler: Akut myeloid lösemi, *Uzun kodlamayan RNA küçük nükleolar RNA konak gen 1*, Tam remisyon, Olaysız sağkalım, Genel sağkalım

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Introduction

Acute myeloid leukemia (AML), with an estimated incidence of 1.62 cases per hundred thousand persons in China [1,2,3], is a genetically heterogeneous disease characterized by the malignant proliferation of undifferentiated myeloid precursors and the inhibition of normal hematopoiesis [4,5]. Although current AML therapy has significantly improved the complete remission (CR) rate [3], the survival profile of AML patients is unfortunately still unsatisfying, with 5-year overall survival (OS) ranging from 20% to 50% [6,7]. Recently, individualized therapy based on risk stratification has been applied for more appropriate regimens and more favorable prognoses for AML patients [6,7]; several novel biomarkers have been identified to date in terms of risk stratification, including t(9:22), *DEK-NUP214*, *KMT2A* rearranged, *BCR-ABL1*, muted *RUNX1*, and muted *ASXL1*, which are recommended for consideration by the National Comprehensive Cancer Network (NCCN) [5,6,7,8,9]. However, efforts to explore new biomarkers related to disease progression and prognosis are still ongoing in hopes of tailoring individual therapy and further improving the prognosis of AML patients.

Long noncoding RNA small nucleolar RNA host gene 1 (*lnc-SNHG1*), which is located on chromosome 11-GRCh38.p13, plays a tumorigenic role in multiple carcinomas [10,11,12,13,14,15]. In terms of solid carcinoma, one study found that *lnc-SNHG1* was associated with worse prognosis in cases of serous epithelial ovarian cancer [15]. Moreover, *lnc-SNHG1* could promote osteosarcoma progression through the miR-577/WNT2B/Wnt/β-catenin axis [10]. Concerning hematological malignancies, a few publications have reported that *lnc-SNHG1* serves as an oncogene in AML. One study showed that elevated *lnc-SNHG1* expression upregulated the proliferation of AML cells via the miR-488-5p/NUP205 pathway [11]. Another study revealed that downregulated *lnc-SNHG1* inhibited AML cell growth by upregulating miR-489-3p to suppress SOX12/Wnt/β-catenin signaling [12]. More importantly, a previous study that included 200 pediatric AML patients revealed that high expression of *lnc-SNHG1* was associated with an elevated risk of leukemogenesis and worse prognosis in these AML patients [13]. Regarding adults, a small study of 89 adult AML patients found that *lnc-SNHG1* facilitated disease progression and indicated poor prognosis [14]. However, the sample sizes of some of these studies were too small to permit firm conclusions and disease controls were lacking.

Thus, in the present study, we recruited 161 patients with de novo AML, 50 patients with nonmalignant hematological disorders, and 50 healthy donors with the aim of assessing the expression of *lnc-SNHG1* in their bone marrow, as well as its clinical value as a potential indicator in adult AML patients.

Materials and Methods

Subjects

Between January 2015 and December 2019, 161 de novo AML patients treated in our hospital were consecutively enrolled in this study. All enrolled patients were newly diagnosed with primary AML by morphological, immunophenotypic, cytogenetic, and molecular genetic examinations and were >18 years of age. Patients were ineligible for enrollment if they had acute promyelocytic leukemia, secondary or relapsed AML, other concomitant hematopoietic malignancies, or pregnancy or lactation. The 50 patients with nonmalignant hematological disorders and the 50 healthy donors were enrolled as the disease control (DC) group and healthy control (HC) group, respectively. The DC group included patients with non-severe aplastic anemia and megaloblastic anemia, which were confirmed by a series of necessary examinations, such as physical examination, laboratory examination, and imaging, and hyperplastic malignancies were excluded. All HC individuals were recruited when they presented for bone marrow donation at the hospital. Both DC and HC individuals were required to be at least 18 years of age with no history of malignancies. In addition, pregnant and lactating women were not included in the DC or HC group. Ethical approval was obtained from the relevant ethics committee. Written informed consent was obtained from all participants.

Sample Collection and Clinical Data Recording

Bone marrow samples were respectively collected from the AML patients (before starting therapy), the DC group (at the time of diagnostic examination), and the HC group (at the

time of donation). Following sample collection, bone marrow mononuclear cells (BMMCs) were isolated by density-gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare Life Sciences, Pittsburgh, PA, USA) and stored at -80 °C until the further determination of *lnc-SNHG1* expression by reverse transcription-quantitative polymerase chain reaction (RT-qPCR). The main clinical characteristics of the AML patients were also recorded after a series of necessary diagnostic examinations.

Evaluation of *lnc-SNHG1*

Quantitative analysis of *lnc-SNHG1* expression in the BMMCs was performed by RT-qPCR assay. The total RNA from the BMMCs was extracted with TRIzol reagent (Thermo Fisher Scientific, Waltham, MA, USA) [16], and the complementary DNA was synthesized using 500 ng of RNA and the PrimeScript RT Reagent Kit (Perfect Real Time, Takara, Dalian, China). PCR was performed using the SYBR Premix DimerEraser (Takara, Dalian, China). *Glyceraldehyde-3-phosphate dehydrogenase* (*GAPDH*) was used as an internal reference for *lnc-SNHG1.* The primers of *ln-SNHG1* were forward 5′-AGGCTGAAGTTACAGGTC-3′ and reverse 5′-TTGGCTCCCAGTGTCTTA-3′, while the primers of *GAPDH* were forward 5′-GAGTCCACTGGCGTCTTCAC-3′ and reverse 5′-ATCTTGAGGCTGTTGTCATACTTCT-3′. The $2^{-\Delta\Delta Ct}$ method was applied to calculate *lnc-SNHG1* relative expression [17]. In detail, the Ct value of the gene was first determined for each sample by calculating the mean Ct value of the gene in three replicates. The original Ct value was then obtained. Finally, the equation of ΔΔCt = ΔCt (test) - ΔCt (calibrator) was applied, where ΔCt (test) = Ct (*lnc-SNHG1* in test sample) - Ct (*GAPDH* in test sample), and ΔCt (calibrator) = Ct (*lnc-SNHG1* in control sample) - Ct (*GAPDH* in control sample). In the current study, the HC sample with the median Ct value of *lnc-SNHG1* expression among all HC samples served as the control sample for the calculation of the relative expression of *lnc-SNHG1*.

Assessment and Follow-Up

All patients in the current study received standard treatment according to the policies of our center. Remission assessment for AML patients was conducted at 21-28 days after starting the standard induction therapy of the "3+7" regimen (3-day anthracycline and 7-day cytarabine or treatments of comparable intensity, as recommended by an international expert panel [18]). The remission criteria were taken from the relevant guidelines [18]. In addition, after induction therapy of the "3+7" regimen, 35 patients underwent allogeneic hematopoietic stem cell transplantation and 86 patients received cytarabine alone or combined with mitoxantrone, fludarabine, or homoharringtonine for consolidation therapy for 3 or 4 cycles. Forty patients who failed to achieve CR after induction therapy received cladribine, cytarabine, and granulocyte colony-stimulating factor (G-CSF) with mitoxantrone or idarubicin; or fludarabine, cytarabine, and G-CSF with or without idarubicin; or high-dose cytarabine combined with idarubicin; or chemotherapy plus target therapy such as decitabine combined with sorafenib. Follow-up appointments for AML patients were held every 1-3 months or as clinically indicated until March 31, 2021. According to the follow-up documents, event-free survival (EFS) and OS were estimated according to the definitions in the relevant guidelines [18].

Statistical Analysis

IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 7.02 (GraphPad Software Inc., San Diego, CA, USA) were used for statistical analysis and figure plotting, respectively. The *lnc-SNHG1* expression of the AML patients was classified into four levels based on expression quantiles: Q1, 0% to 25%; Q2, 26% to 50%; Q3, 51% to 75%; and Q4, 76% to 100%. As appropriate, comparative analyses were checked by the Wilcoxon rank-sum test, Kruskal-Wallis H rank-sum test, one-way analysis of variance (ANOVA), or chi-square test. Receiver operating characteristic (ROC) curve analysis was conducted to assess the performance of variables in differentiating different subjects. The Kaplan-Meier method and log-rank test were used to analyze the EFS and OS among AML patients. Values of $p<0.05$ indicated statistical significance, while in multiple comparisons, Bonferroni correction was applied to adjust the significance level to $\alpha<0.008$ ($p<0.008$).

Results

Characteristics of AML Patients

The age of the AML patients was 57.9±12.3 years (Table 1). There were 98 (60.9%) male and 63 (39.1%) female AML patients. The median white blood cell (WBC) count was 14.3 (8.0-27.7)x10^9/L. The mean percentage of bone marrow blasts was 72.9±14.5%. In terms of FAB classification, 10 (6.2%) patients were classified as M1, 49 (30.4%) patients as M2, 44 (27.3%) patients as M4, and 58 (36.0%) patients as M5. More detailed information is given in Table 1.

Comparison of *lnc-SNHG1* Expression Among AML, DC, and HC Groups

Lnc-SNHG1 expression varied among AML patients and the DC and HC groups ($p<0.001$, Figure 1A). The AML patients had the highest *lnc-SNHG1* expression at 2.612 (1.660-3.125), followed by the DC group with *lnc-SNHG1* expression of 1.630 (1.098-2.059). *Lnc-SNHG1* expression was lowest at 0.992 (0.831-1.455) in the HC group. Subgroup comparisons illustrated that *lnc-SNHG1* expression was higher in AML patients than in the DC and HC groups (both $p<0.001$). Meanwhile, an ROC curve was drawn to distinguish the AML patients from the DC and HC groups (Figure 1B), and *lnc-SNHG1* expression was found to be related to AML risk with area under the curve (AUC) of 0.726 [95% confidence interval (CI): 0.649-0.802] versus DC and 0.884 (95% CI: 0.838-0.931) versus HC.

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Correlation of *lnc-SNHG1* expression with clinical characteristics

Lnc-SNHG1 expression was only positively correlated with WBC count (p=0.008, Table 2). It was not correlated with age (p=0.260), gender (p=0.581), bone marrow blasts (p=0.070), FAB classification (p=0.852), cytogenetics (p=0.190), monosomal karyotype (p=0.463), internal tandem duplications in the *FMS-like tyrosine kinase 3* (*FLT3-ITD*) mutation (p=0.108), isolated biallelic *CCAAT/enhancer-binding protein* α (isolated biallelic *CEBPA*) mutation (p=0.297), *nucleophosmin 1* (*NPM1*) mutation (p=0.190), *Wilms tumor* (*WT1*) mutation (p=0.247), or NCCN risk stratification (p=0.105). More detailed information is provided in Table 2.

Table 1. Characteristics of AML patients.

Variables	AML patients (n=161)
Age (years), mean±SD	57.9±12.3
Gender, n (%)	
Male	98 (60.9)
Female	63 (39.1)
WBC (x10^9/L), median (IQR)	14.3 (8.0-27.7)
BM blasts (%), mean±SD	72.9±14.5
FAB classification, n (%)	
M1	10 (6.2)
M2	49 (30.4)
M4	44 (27.3)
M5	58 (36.0)
Cytogenetics, n (%)	
NK	78 (48.4)
CK	20 (12.4)
inv(16) or t(16;16)	11 (6.8)
+8	7 (4.3)
t (9;11)	6 (3.7)
-7 or 7q-	6 (3.7)
-5 or 5q-	1 (0.6)
t(8; 21)	1 (0.6)
Others (not defined)	31 (19.3)
MK, n (%)	11 (6.8)
FLT3-ITD mutation, n (%)	39 (24.2)
Isolated biallelic *CEBPA* mutation, n (%)	16 (9.9)
NPM1 mutation, n (%)	45 (28.0)
WT1 mutation, n (%)	20 (12.4)
Risk stratification, n (%)	
Better	31 (19.3)
Intermediate	83 (51.6)
Poor	47 (29.2)

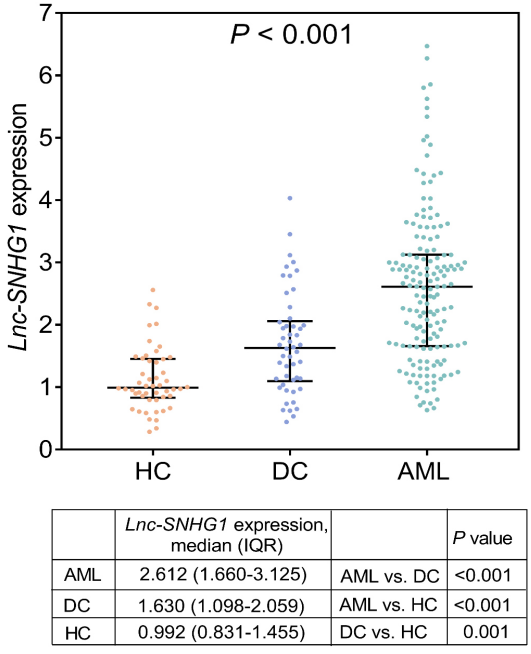
AML: Acute myeloid leukemia; SD: standard deviation; WBC: white blood cell count; IQR: interquartile range; BM: bone marrow; FAB classification: French-American-British classification; NK: normal karyotype; CK: complex karyotype; MK, monosomal karyotype; *FLT3-ITD*: *internal tandem duplications in the FMS-like tyrosine kinase 3*; *CEBPA*: *CCAAT/enhancer-binding protein* α; *NPM1*: *nucleophosmin 1*; *WT1*: *Wilms tumor 1*.

Comparison of CR Rates Among Different *lnc-SNHG1* Expression Levels

In general, CR rates varied among patients with different *lnc-SNHG1* expression levels (p=0.001, Figure 2). More specifically, 37 (92.5%), 33 (82.5%), 29 (70.7%), and 22 (55%) patients with *lnc-SNHG1* expression at the Q1, Q2, Q3, and Q4 levels achieved CR. Compared to patients with *lnc-SNHG1* expression at Q1 (p=0.001) and Q2 (p=0.008), patients with *lnc-SNHG1* expression at Q4 had worse CR rates. Moreover, patients with *lnc-SNHG1* expression at Q3 had lower CR rates than those with *lnc-SNHG1* expression at Q1 (p=0.012). Other intergroup comparisons yielded no significant differences (all p>0.05).

Correlation of *lnc-SNHG1* Expression with EFS and OS

Generally, *lnc-SNHG1* expression was negatively correlated with longer EFS (p<0.001, Figure 3). Patients with *lnc-SNHG1* expression at Q4 had worse EFS compared to those with *lnc-SNHG1* expression at Q1 (p<0.001), Q2 (p=0.001), and Q3 (p=0.025), respectively. Other subgroup comparisons yielded no significant differences (all p>0.05).



	Lnc-SNHG1 expression, median (IQR)		*P* value
AML	2.612 (1.660-3.125)	AML vs. DC	<0.001
DC	1.630 (1.098-2.059)	AML vs. HC	<0.001
HC	0.992 (0.831-1.455)	DC vs. HC	0.001

Figure 1. Comparison of *lnc-SNHG1* expression and ROC curve analysis. *Lnc-SNHG1* expression comparison among HC, DC, and AML groups, with each dot indicating the *lnc-SNHG1* expression of each sample (**A**). ROC curve distinguishing AML patients from HC and DC groups (**B**). DC: Disease control; HC: healthy control; AML: acute myeloid leukemia; *Lnc-SNHG1: long noncoding RNA small nucleolar RNA host gene 1*; IQR: interquartile range; ROC: receiver operating characteristic (Wilcoxon rank-sum test, Kruskal-Wallis H rank-sum test, and ROC curve analysis were used).

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Table 2. Comparison of clinical characteristics among AML patients with different quantile expressions of *lnc-SNHG1*.

Items	*Lnc-SNHG1* expression				
	Q1	Q2	Q3	Q4	p
Age (years), mean ± SD	55.5±10.3	59.1±13.5	56.7±13.6	60.4±11.3	0.260
Gender, n (%)					0.581
Male	21 (52.5)	25 (62.5)	25 (61.0)	27 (67.5)	
Female	19 (47.5)	15 (37.5)	16 (39.0)	13 (32.5)	
WBC (x10^9/L), median (IQR)	11.3 (4.5-22.9)	12.0 (5.2-23.7)	20.2 (10.9-31.0)	21.9 (11.5-28.3)	0.008
BM blasts (%), mean ± SD	69.2±14.4	71.4±14.5	73.5±15.5	77.4±12.5	0.070
FAB classification, n (%)					0.852
M1	2 (5.0)	2 (5.0)	3 (7.3)	3 (7.5)	
M2	12 (30.0)	13 (32.5)	9 (22.0)	15 (37.5)	
M4	12 (30.0)	13 (32.5)	10 (24.4)	9 (22.5)	
M5	14 (35.0)	12 (30.0)	19 (46.3)	13 (32.5)	
Cytogenetics, n (%)					0.190
NK	16 (40.0)	21 (52.5)	21 (51.2)	20 (50.0)	
CK	6 (15.0)	3 (7.5)	6 (14.6)	5 (12.5)	
inv(16) or t(16;16)	3 (7.5)	7 (17.5)	0 (0.0)	1 (2.5)	
+8	1 (2.5)	1 (2.5)	4 (9.8)	1 (2.5)	
t(9;11)	1 (2.5)	1 (2.5)	2 (4.9)	2 (5.0)	
-7 or 7q-	2 (5.0)	3 (7.5)	1 (2.4)	0 (0.0)	
-5 or 5q-	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	
t(8; 21)	1 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	
Others (not defined)	9 (22.5)	4 (10.0)	7 (17.1)	11 (27.5)	
MK, n (%)					0.463
Yes	2 (5.0)	4 (10.0)	4 (9.8)	1 (2.5)	
No	38 (95.0)	36 (90.0)	37 (90.2)	39 (97.5)	
FLT3-ITD mutation, n (%)					0.108
Yes	6 (15.0)	8 (20.0)	10 (24.4)	15 (37.5)	
No	34 (85.0)	32 (80.0)	31 (75.6)	25 (62.5)	
Isolated biallelic *CEBPA* mutation, n (%)					0.297
Yes	3 (7.5)	4 (10.0)	7 (17.1)	2 (5.0)	
No	37 (92.5)	36 (90.0)	34 (82.9)	38 (95.0)	
NPM1 mutation, n (%)					0.190
Yes	9 (22.5)	16 (40.0)	12 (29.3)	8 (20.0)	
No	31 (77.5)	24 (60.0)	29 (70.7)	32 (80.0)	
WT1 mutation, n (%)					0.247
Yes	5 (12.5)	2 (5.0)	5 (12.2)	8 (20.0)	
No	35 (87.5)	38 (95.0)	36 (87.8)	32 (80.0)	
Risk stratification, n (%)					0.105
Better	9 (22.5)	15 (37.5)	4 (9.8)	3 (7.5)	
Intermediate	19 (47.5)	15 (37.5)	24 (58.5)	25 (62.5)	
Poor	12 (30.0)	10 (25.0)	13 (31.7)	12 (30.0)	

AML: Acute myeloid leukemia; *Lnc-SNHG1: long noncoding RNA small nucleolar RNA host gene 1*; SD: standard deviation; WBC: white blood cell count; IQR: interquartile range; BM: bone marrow; FAB classification: French-American-British classification; NK: normal karyotype; CK: complex karyotype; MK, monosomal karyotype; *FLT3-ITD: internal tandem duplications in the FMS-like tyrosine kinase 3; CEBPA: CCAAT/enhancer-binding protein* α; *NPM1: nucleophosmin 1; WT1: Wilms tumor 1.*

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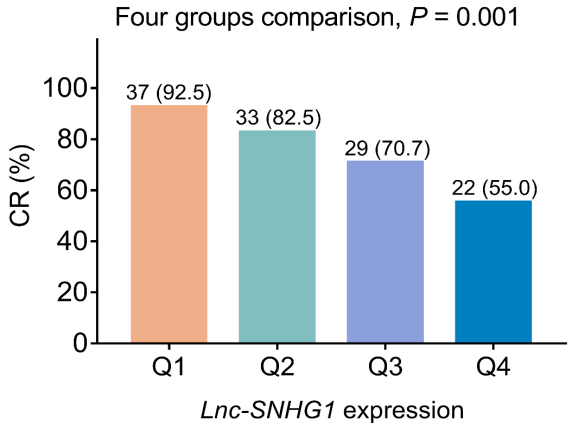
Furthermore, *lnc-SNHG1* expression was negatively correlated with longer OS (p=0.002, Figure 4). Patients with *lnc-SNHG1* expression at Q4 had worse OS compared to patients with *lnc-SNHG1* expression at Q1 (p<0.001), Q2 (p=0.013), and Q3 (p=0.041), respectively. Other subgroup comparisons yielded no significant differences (all p>0.05).

Additionally, multivariate Cox proportional hazards regression analysis revealed that high *lnc-SNHG1* expression was independently linked with poor EFS (p=0.001) and OS (p=0.007) in AML patients (Table 3). Both the NCCN risk stratification and *lnc-SNHG1* expression could predict shorter EFS and OS.

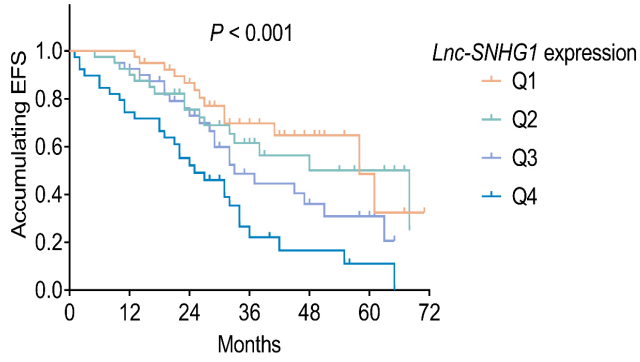


Post-hoc multiple comparisons	*P* value
Q4 vs. Q1	0.001
Q4 vs. Q2	0.008
Q4 vs. Q3	0.143
Q3 vs. Q1	0.012
Q3 vs. Q2	0.211
Q2 vs. Q1	0.176

Figure 2. Correlation of *lnc-SNHG1* expression with CR rate. CR: Complete remission; Q: quartile; *Lnc-SNHG1*: *long noncoding RNA small nucleolar RNA host gene 1* (one-way analysis of variance was used).

Discussion

Lnc-SNHG1 has been reported to play a critical role in multiple carcinomas via mediating multiple pathways. In solid carcinomas, *lnc-SNHG1* functions as a tumor-promoting gene [10,19]. A previous study found that SNHG1 knockdown inhibited tumor growth and metastasis in hepatocellular carcinoma through downregulation of the FOXK1/Snail axis [19]. *Lnc-SNHG1* overexpression was also correlated with larger tumor size and more advanced TNM stage in osteosarcoma via activation of the WNT2B/Wnt/β-catenin axis [10]. Prior studies illustrated that *lnc-SNHG1* promoted disease progression via numerous signaling pathways in cases of hematological malignancies, and especially AML [11,12]. Increased *lnc-SNHG1* expression



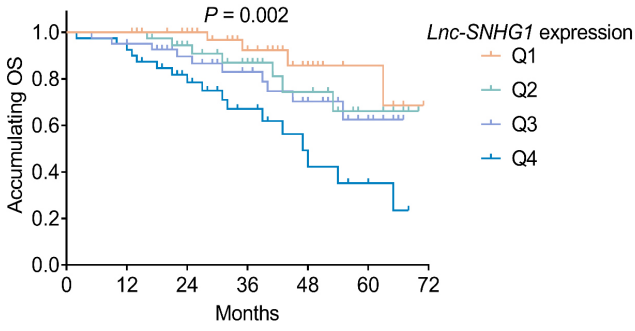
Multiple comparisons	*P* value
Q4 vs. Q1	<0.001
Q4 vs. Q2	0.001
Q4 vs. Q3	0.025
Q3 vs. Q1	0.054
Q3 vs. Q2	0.172
Q2 vs. Q1	0.463

Figure 3. Correlation of *lnc-SNHG1* expression with EFS. EFS: Event-free survival; Q: quartile; *Lnc-SNHG1*: *long noncoding RNA small nucleolar RNA host gene 1* (Kaplan-Meier method and log-rank test were used).

Table 3. Multivariate Cox proportional hazards regression analysis for EFS and OS.

Items	p	HR	95% CI	
			Lower	Upper
Multivariate Cox regression analysis for EFS				
High *lnc-SNHG1*	0.001	1.456	1.172	1.807
High WBC	<0.001	1.029	1.017	1.042
Poor risk stratification	0.001	1.831	1.286	2.609
Multivariate Cox regression analysis for OS				
High *lnc-SNHG1*	0.007	1.580	1.130	2.208
High WBC	0.018	1.022	1.004	1.040
Isolated biallelic *CEBPA* mutation	0.024	0.181	0.041	0.802
Poor risk stratification	<0.001	3.775	2.079	6.854

EFS: Event-free survival; OS: overall survival; HR: hazard ratio; CI: confidence interval; *lnc-SNHG1*: *long noncoding RNA small nucleolar RNA host gene 1*; WBC: white blood cell count; *CEBPA*: *CCAAT/enhancer-binding protein* α.



Multiple comparisons	*P* value
Q4 vs. Q1	<0.001
Q4 vs. Q2	0.013
Q4 vs. Q3	0.041
Q3 vs. Q1	0.116
Q3 vs. Q2	0.636
Q2 vs. Q1	0.290

Figure 4. Correlation of *lnc-SNHG1* expression with accumulating OS. OS: Overall survival; Q: quartile; *Lnc-SNHG1*: *long noncoding RNA small nucleolar RNA host gene 1* (Kaplan-Meier method and log-rank test were used).

facilitated the proliferation of AML cells through the miR-488-5p/NUP205 axis [11]. Similarly, another study illustrated that *lnc-SNHG1* promoted AML cell proliferation by suppressing miR-489-3p/SOX12/Wnt/β-catenin signaling [12].

Previous clinical studies showed that *lnc-SNHG1* was highly expressed in AML patients. One study illustrated that *lnc-SNHG1* was highly expressed in juvenile AML patients [13]. It was also found to be highly expressed in AML cell lines in vitro, with another study revealing that *lnc-SNHG1* was highly expressed in primary AML cells and THP-1 cells [11,12]. In our study, *lnc-SNHG1* expression in AML patients was higher than that observed in members of the DC and HC groups, with good value in distinguishing AML patients from DC and HC individuals. According to the evidence presented above, a possible explanation could be that increased *lnc-SNHG1* expression indicates a high cellular proliferation speed, with the proliferation rate of AML cells being higher than that of normal myeloid cells; thus, *lnc-SNHG1* is highly expressed in AML patients [11,12].

In terms of the correlation between *lnc-SNHG1* and clinical features, it was found that increased expression of *lnc-SNHG1* was correlated with worse clinical index scores and risk stratification in juvenile AML patients [13]. The present study showed that increased *lnc-SNHG1* expression was associated with elevated WBC count, resulting in *lnc-SNHG1* facilitating the proliferation of AML cells [11,12,13]. Therefore, elevated *lnc-SNHG1* could be related to worsened AML features. In addition, worse AML status is linked to elevated WBC counts, and *lnc-SNHG1* could thus be further associated with elevated WBC counts.

The present study also demonstrated that *lnc-SNHG1* expression was negatively correlated with CR rates and survival profiles in AML patients. The underlying reasons for this are as follows: 1) Since *lnc-SNHG1* promotes proliferation while inhibiting the apoptosis of AML cells, *lnc-SNHG1* is correspondingly correlated with lower CR rates and worse survival profiles in AML patients. 2) *Lnc-SNHG1* might reduce the chemosensitivity of AML patients to chemotherapy; thus, *lnc-SNHG1* leads to lower CR rates and worse survival profiles in AML patients [15,20,21]. However, the specific mechanisms need further investigation.

Study Limitations

There were some limitations of this study. First, since this was a single-center study, there may have been selection bias, which would influence the applicability of our findings. Second, all AML patients enrolled in this study were newly diagnosed. Therefore, these findings might not be generalizable for secondary or relapsed AML. Third, the potential mechanism by which *lnc-SNHG1* regulates the pathogenesis of AML remains unclear and it needs to be explored in future research. Thus, it is too early to assert that *lnc-SNHG1* could definitely serve as a prognostic indicator for AML patients.

Conclusion

Collectively, *lnc-SNHG1* is highly expressed in AML patients, and its overexpression correlates with elevated WBC counts, poor induction treatment responses, and poor survival profiles in AML patients. It may potentially serve as an indicator for AML.

Ethics

Ethics Committee Approval: Ethics approval was obtained from the relevant ethics committee.

Informed Consent: Written informed consent was obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: P.Z., Y.C.; Concept: P.Z., Y.C., C.Y.; Design: P.Z., Y.C., C.Y.; Data Collection or Processing: L.Y., C.W., H.C., L.L., J.L., H.L.; Analysis or Interpretation: P.Z., Y.Z., T.C., Y.L., W.H.; Literature Search: L.Y., C.W., H.C., L.L., J.L., H.L., Y.Z., T.C., Y.L., W.H.; Writing: P.Z., Y.C., C.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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