Original Article

Novel cuproptosis-related lncRNAs can predict the prognosis of patients with multiple myeloma

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Background: Cuproptosis-related long-stranded non-coding RNAs (lncRNAs) have several implications for the prognosis of multiple myeloma (MM). This research aimed to construct a prognostic risk model for MM patients and explore the potential signaling pathways in the risk group.

Methods: Cuproptosis-related lncRNAs were obtained from the co-expression analysis of cuproptosis-related genes and lncRNAs. Subsequently, twelve cuproptosis-related lncRNAs were selected to construct a prognostic risk model of MM patients by the least absolute shrinkage and selection operator (LASSO) regression. Then, the clinical data of these patients were randomly divided into the training group and the testing group. Next, patients were divided into the low- and high-risk groups according to the median risk score. The Kaplan-Meier survival analysis was performed to clarify the prognostic differences between risk subtypes. Besides, the Cox analysis was conducted to identify whether the risk score can be used as an independent prognostic factor. In addition, the receiver operating characteristic (ROC) curve analysis and the concordance index (C-index) curve analysis were performed to elucidate the value of risk score as a prognostic indicator. Finally, the differential risk analysis and functional enrichment analysis were carried out to identify the potential signaling pathways in the low- and high-risk groups.

Results: The results demonstrated that the overall survival (OS) of patients in the high-risk group was shorter than that in the low-risk group. There were significant differences in the expression of genes in MM patients between the high- and low-risk groups. The Gene Ontology (GO) analysis results showed that the differentially expressed risk-related genes (DERGs) were mainly concentrated on the collagen-containing extracellular matrix. According to the Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis results, the DERGs may be related to the neuroactive ligand-receptor interaction and mitogen-activated protein kinase (MAPK) signaling pathway, indicating that they may be involved in the progression of tumors.

Conclusions: The findings of this study suggest that cuproptosis-related lncRNAs may be effective biomarkers for predicting the prognosis of MM patients, which is anticipated to contribute to the improvement of clinical outcomes.

Keywords: Multiple myeloma (MM); cuproptosis-related long-stranded non-coding RNA (cuproptosis-related lncRNA); prognosis; differential risk analysis

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Introduction

Multiple myeloma (MM) is a hematological malignant tumor caused by abnormal proliferation of plasma cells in the bone marrow. The most common manifestations of MM include hypercalcemia (1,2), renal failure (3,4), anemia (5,6), and lytic bone lesions (7,8), which mainly affect the elderly population (9). The high-dose therapy (HDT), autologous stem cell transplantation (ASCT), and the emergence of new drugs (such as bortezomib and thalidomide) have improved the survival rate of MM patients (10). However, almost all MM patients would suffer a relapse (11-13).

As a basic nutrient, copper can exert both beneficial and toxic effects on cells due to its redox properties (14,15). Intracellular copper concentration is maintained at a very low level through an active steady-state working mechanism across concentration gradients (16). Different from the known programmed cell death (such as ferroptosis and apoptosis), copper ionophore-induced cell death is closely related to mitochondrial respiration and protein lipoylation (17-19). In this process, copper binds directly to the lipoylated components of the tricarboxylic acid (TCA) cycle, which leads to the accumulation of lipoylated proteins and the subsequent loss of iron-sulfur cluster proteins. This induces protein toxic stress and eventually leads to cell death (20). In addition, it was demonstrated in a recent study that high anti-MM efficacy was showed in treatment-resistant cellular models of MM patients, when using copper ionophores (21).

Long-stranded non-coding RNAs (lncRNAs) is a group of RNA molecules with a transcriptional length more than 200 nT. They are initially considered to be false transcriptional noise caused by low RNA polymerase fidelity (22). The promoter region of lncRNAs is generally more conservative than that of messenger RNAs (mRNAs). Different from mRNAs, lncRNAs do not encode proteins. However, lncRNAs can regulate gene expression in the form of RNA at multiple epigenetic, transcriptional and post-transcriptional levels (23). LncRNAs can induce many important cancer phenotypes by interacting with other cellular macromolecules, DNAs, proteins, and RNAs (24). Some lncRNAs have been shown to regulate apoptosis (25,26), ferroptosis (27-29), and cuproptosis (30,31) of cancer cells. Furthermore, the expression of lncRNAs usually changes and is related to the prognosis of various cancer patients. Mounting evidence supports the independent prognostic value of lncRNAs in patients with MM, leading to the development of multiple prognostic lncRNA signatures (32,33).

LncRNAs participate in tumor progression by regulating cuproptosis genes. Numerous studies have focused on molecular classification and survival prediction using lncRNAs. One study (34) constructed a cuproptosis-related lncRNAs prognosis prediction model, which can reliably and accurately predict the prognosis, drug sensitivity, and clinical recurrence of acute myeloid leukaemia. However, there is no research on the relationship between the prognosis and score in MM based on cuproptosis-related lncRNAs, and whether it can be used as an independent prognostic factor is not clear. Therefore, we analyzed the data with a view to exploring cuproptosis-related lncRNAs biomarkers to predict the prognosis of MM patients.

In this study, a bioinformatics analysis method was used to construct a prognostic risk model for MM patients based on the cuproptosis-related lncRNA score. Moreover, the differential risk analysis and functional enrichment analysis were also conducted to identify the potential signaling pathways in the risk group. These findings are expected to provide some theoretical support for exploring the regulation of cuproptosis-related lncRNAs in MM. The flow chart of this research is sketched in *Figure 1*. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-960/rc).

Highlight box

Key findings

- A prognostic model consisting of twelve cuproptosis-related long-stranded non-coding RNAs (lncRNAs) was a strong predictor of multiple myeloma (MM).

What is known and what is new?

- Cuproptosis-related lncRNAs play a key role in MM development and metastasis.
- Cuproptosis-related lncRNAs were used to construct a prognostic model, and the new model was found to be associated with the prognosis of MM.

What is the implication, and what should change now?

- This study highlights the importance of cuproptosis-related lncRNAs in predicting prognosis in MM.

Methods

Data acquisition and preprocessing

In order to identify cuproptosis-related lncRNAs that can

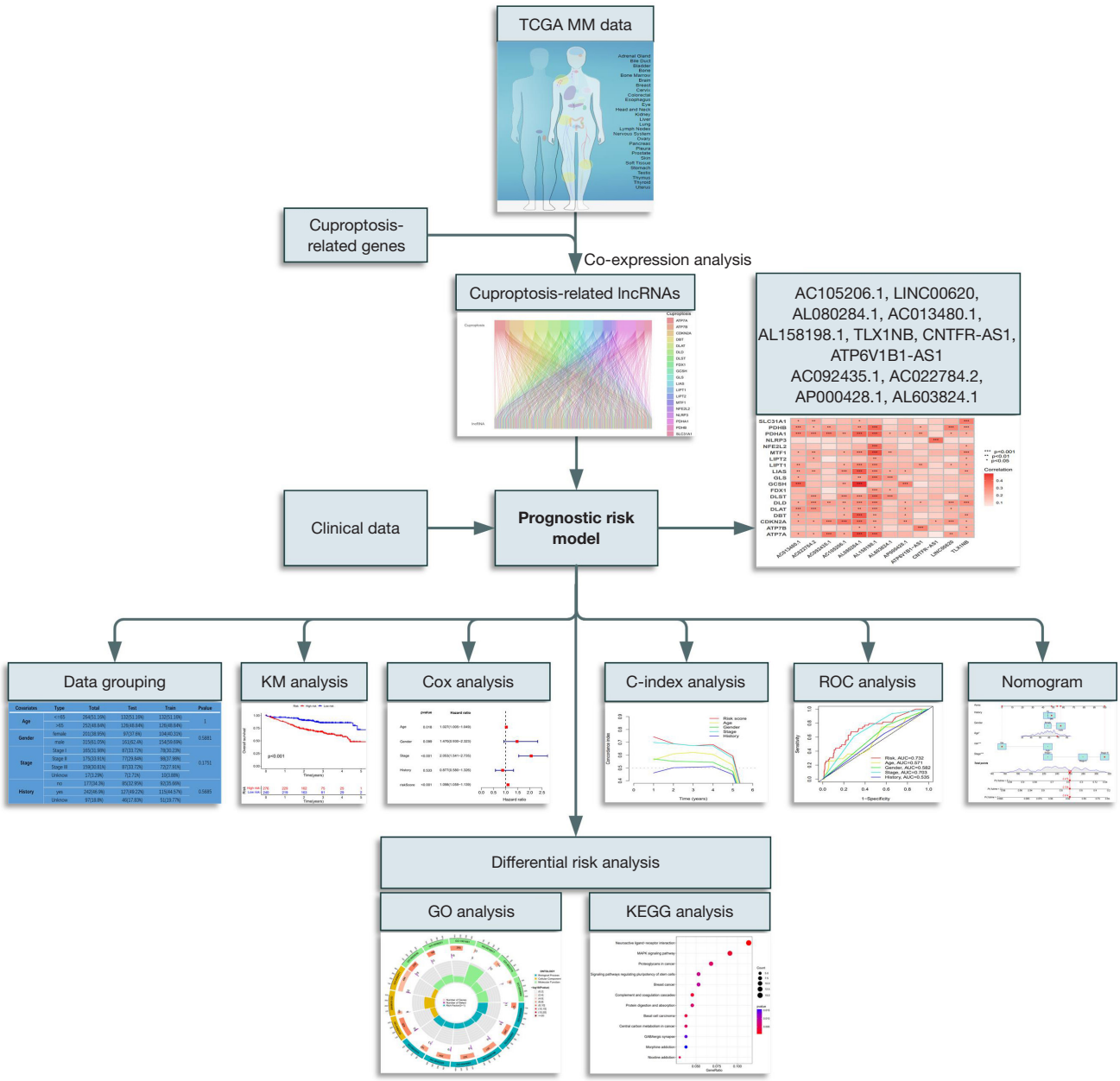

Figure 1 The schematic flow chart of this research. TCGA, The Cancer Genome Atlas; MM, multiple myeloma; lncRNAs, long-stranded non-coding RNAs; KM, Kaplan-Meier; C-index, concordance index; ROC, receiver operating characteristic; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.

be employed to predict the prognosis of MM patients, this study was conducted based on the following four points.

(I) The expression profile was obtained by array or high-throughput sequencing.

(II) Data samples were collected from MM patients diagnosed for the first time.

(III) More than 300 cases were included to constitute a meaningful sample size.

(IV) The data were the count files obtained by RNA sequencing (RNA-Seq) in gene expression quantification.

The expression profile data and clinical data of MM

(MMRF-COMMPASS) were downloaded from the Cancer Genome Atlas (TCGA) database (https://portal.gdc.cancer.gov/), and then lncRNAs were identified according to the gene annotation of TCGA. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Cuproptosis-related genes were collected from a series of recent reports (35-38), including *NFE2L2*, *NLRP3*, *ATP7A*, *ATP7B*, *SLC31A1*, *FDX1*, *LIAS*, *LIPT1*, *LIPT2*, *DLD*, *DLAT*, *PDHA1*, *PDHB*, *MTF1*, *GLS*, *CDKN2A*, *DBT*, *GCSH*, and *DLST*. Combined with the standardized gene expression matrix, the cuproptosis-related gene expression matrix was obtained. Finally, the potential cuproptosis-related lncRNAs were identified based on the co-expression analysis of the cuproptosis-related genes expression matrix and the lncRNA expression matrix with the aid of the limma package in R software, with a correlation coefficient larger than 0.3 and P value less than 0.001 as screening conditions.

Construction of a prognostic risk model by the least absolute shrinkage and selection operator (LASSO) regression

First of all, the sample data of MM patients were randomly divided into the training group and the testing group. Then, cuproptosis-related lncRNAs were screened out by the univariate LASSO regression in the glmnet package in R software (P<0.05). After redundant genes were removed, the remaining cuproptosis-related lncRNAs were used to construct a prognostic risk model. The risk score of each patient was identified according to the expression of the 12 cuproptosis-related lncRNAs and the risk coefficient. The risk score was calculated as follows: (0.370160265859127 × AC105206.1) + (0.430732849678822 × LINC00620) + (0.932090945670286 × AL080284.1) + (0.735909366869273 × AC013480.1) + (0.639619158470217 × AL158198.1) + (0.40164431674857 × TLX1NB) + (–2.18823271531587 × CNTFR-AS1) + (–0.2783376598488 × ATP6V1B1-AS1) + (0.398459050292138 × AC092435.1) + (0.313821766142159 × AC022784.2) + (0.317809597431966 × AP000428.1) + (0.395740225449718 × AL603824.1).

Subsequently, a multivariate Cox model was constructed with these selected cuproptosis-related lncRNAs related for the prognosis and survival prediction. Besides, the risk scores of all MM patients were calculated. These patients were divided into the low- and high-risk groups according to the median value of risk scores for prognosis assessment. Furthermore, the Kaplan-Meier survival curves of MM patients in the low- and high-risk groups of the training group and testing group were plotted.

Independent prognostic analysis of the prognostic risk model

The univariate and multivariate Cox analyses were performed to evaluate the effects of risk score, age, gender, International Staging System (ISS) stage, and family tumor history on the prognosis of MM patients. And the variable in the Cox model has respected the hazards proportionality. Then a forest map was plotted. In order to verify the accuracy of this model in predicting the prognosis and survival of MM patients, the survival and timeROC packages in R software were used to calculate the factors of the risk score model and the 1-, 3-, and 5-year area under the curve (AUC). Besides, the C-index curve was constructed.

Construction of nomogram of clinical subgroups

The survival, regplot and rms packages in R software were used to construct a nomogram of clinical subgroups to identify the 1-, 3-, and 5-year survival rates of these MM patients. The nomogram of clinical subgroups was constructed based on the risk score, age, gender, ISS stage, and family history of these MM patients.

Differential risk analysis

With the aid of the limma package in R software, the differentially expressed risk-related genes (DERGs) in the samples of MM patients in the low- and high-risk groups were screened under the condition of |log2FC| >1 and P<0.05.

Functional enrichment analysis

The functional enrichment analysis of DERGs was carried out by GO and KEGG through the clusterProfiler package in R software. The results were screened according to corrected P (adj.P)<0.01 to identify the potential signaling pathways in the risk group.

Statistical analysis

The R software is used for data analysis and graphics rendering. The survival curve was drawn using R software

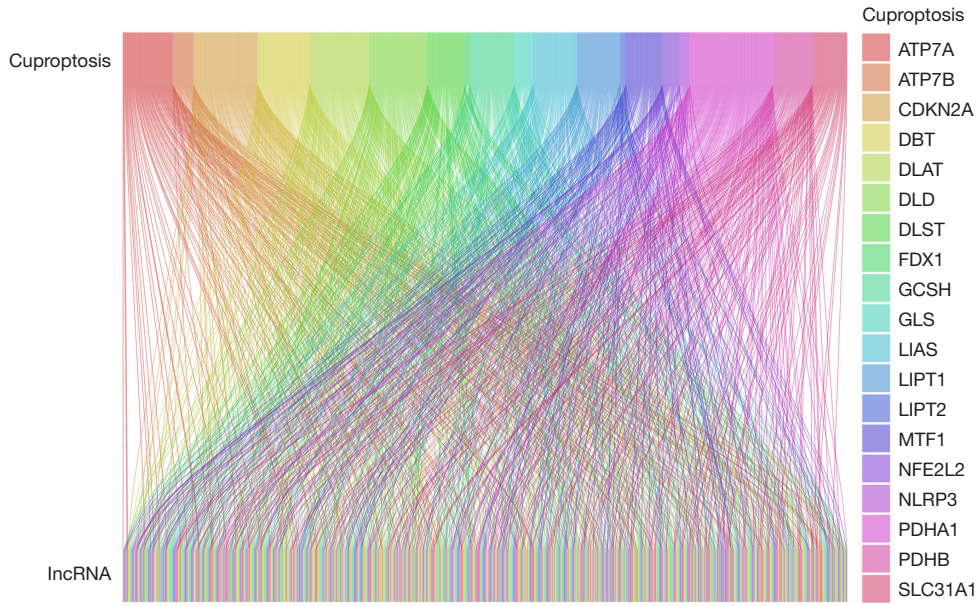

Figure 2 Sankey diagram of the co-expression relationship between cuproptosis-related genes and cuproptosis-related lncRNAs. lncRNA, long-stranded non-coding RNA.

package "survival", and the difference in prognosis between groups was analyzed using survival function in the R software package. Receiver operating characteristic (ROC) analysis was performed using the R software package "timeROC" to obtain the AUC. Nomograms were established using the R the software package "rms" to assess the prognostic significance of some of the features in the samples. P<0.05 indicated that the difference was statistically significant.

Results

Cuproptosis-related lncRNA data acquisition

The bone marrow tissue transcriptome data of 575 MM patients and the clinical data of 516 MM patients were downloaded from the TCGA database (https://portal.gdc.cancer.gov/). Based on the Gencode Database, 16,901 lncRNAs were selected from the TCGA Multiple Myeloma Database. Then, the matrix expression of lncRNAs and cuproptosis-related genes was analyzed under the screening conditions of a correlation coefficient larger than 0.3 and P value less than 0.001. Finally, a total of 294 cuproptosis-related lncRNAs were screened out. The co-expression relationship between cuproptosis-related genes and cuproptosis-related lncRNAs was visualized by the Sankey diagram (*Figure 2*).

Construction of prognostic risk model for MM patients

Firstly, due to lack of related data such as the initial treatment regimen, treatment response, and status of stem cell transplantation, the clinical data of 516 MM patients were randomly divided into the training group and the testing group (*Table 1*). Besides, 294 cuproptosis-related lncRNAs were screened by the univariate Cox analysis (P<0.05), and a total of 76 cuproptosis-related lncRNAs were found to be associated with the survival of MM patients. Additionally, 12 independent prognostic cuproptosis-related lncRNAs were screened according to multivariate Cox analysis.

The relationship between cuproptosis-related genes and lncRNAs was presented in a heatmap (*Figure 3*). According to the median risk score, patients with the risk score lower than the median were classified as the low-risk group, and those with the risk score higher than the median were classified as the high-risk group. It was found that in the training group, the testing group, and all groups, the overall survival (OS) of patients in the high-risk group was shorter than that in the low-risk group (*Figure 4A-4C*).

Independent prognostic analysis of factors and evaluation of the accuracy of the prognostic model

The univariate and multivariate Cox regression analyses can

Table 1 Statistical analysis of clinical data in training group and testing group

Covariates	Type	Total	Test	Train	P value
Age (years)	≤65	264 (51.16)	132 (51.16)	132 (51.16)	>0.99
	>65	252 (48.84)	126 (48.84)	126 (48.84)	
Gender	Female	201 (38.95)	97 (37.6)	104 (40.31)	0.5881
	Male	315 (61.05)	161 (62.4)	154 (59.69)	
Stage	Stage I	165 (31.98)	87 (33.72)	78 (30.23)	0.1751
	Stage II	175 (33.91)	77 (29.84)	98 (37.98)	
	Stage III	159 (30.81)	87 (33.72)	72 (27.91)	
	Unknown	17 (3.29)	7 (2.71)	10 (3.88)	
History	No	177 (34.3)	85 (32.95)	92 (35.66)	0.5685
	Yes	242 (46.9)	127 (49.22)	115 (44.57)	
	Unknown	97 (18.8)	46 (17.83)	51 (19.77)	

Data are presented in n (%).

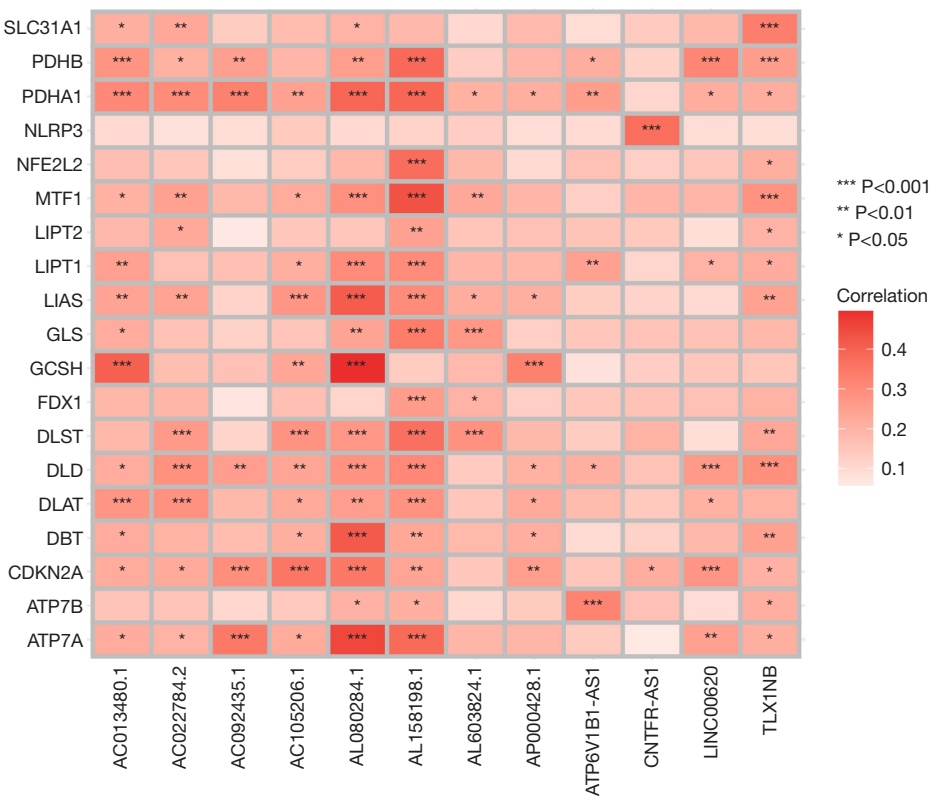

Figure 3 The correlation heatmap of the relationship between cuproptosis-related genes and lncRNAs. lncRNAs, long-stranded non-coding RNAs.

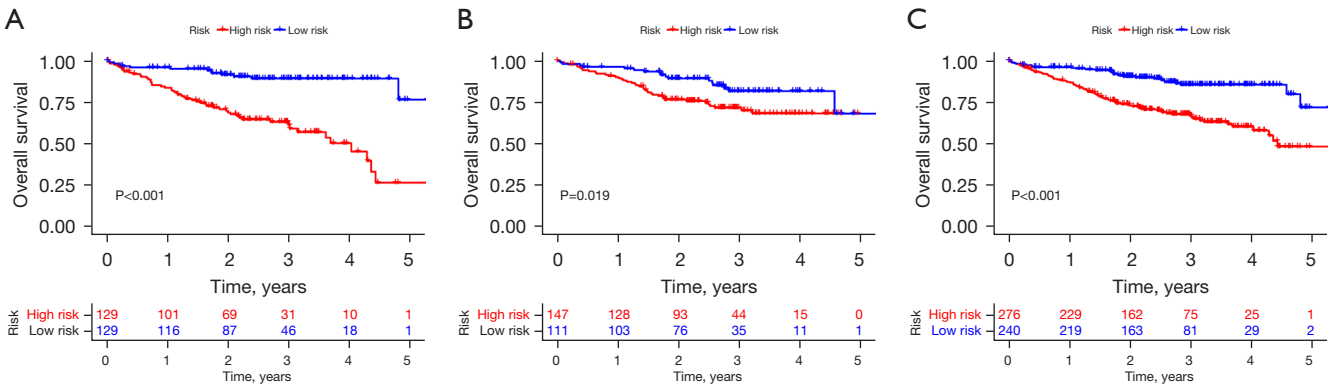

Figure 4 Kaplan-Meier survival analysis results of patients. OS of patients in (A) the training group (B) the testing group, and (C) all groups. OS, overall survival.

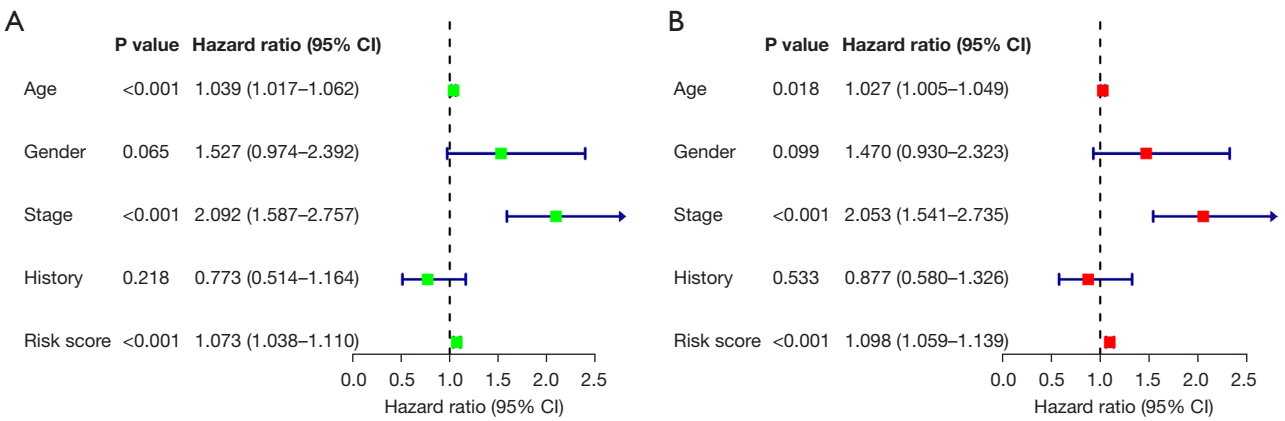

Figure 5 Cox independent prognostic analysis. (A) Univariate; (B) multivariate.

be employed to identify whether the risk score calculated can be used as an independent prognostic factor. Due to the lack of related data of the serum lactate dehydrogenase (LDH) level and high-risk cytogenetics, we constructed the univariate and multivariate Cox regression analysis with age, gender, ISS stage, tumor family history and risk score. The univariate Cox analysis results showed that the age [hazard ratio (HR) =1.039, 95% CI: 1.017–1.062, P<0.001], stage (HR =2.092, 95% CI: 1.587–2.757, P<0.001), and risk score (HR =1.073, 95% CI: 1.038–1.110, P<0.001) of MM patients were correlated with the OS of MM patients (*Figure 5A*). The multivariate Cox analysis results showed that the age (HR =1.027, 95% CI: 1.005–1.049, P=0.018), stage (HR =2.053, 95% CI: 1.541–2.735, P<0.001), and risk score (HR =1.098, 95% CI: 1.059–1.139, P<0.001) were independently correlated with the OS of these patients (*Figure 5B*). This finding suggested that these prognostic factors are independent in MM patients. Then, the ROC curve was employed to evaluate the prediction accuracy of the risk score. On the one hand, the AUC of risk score was 0.732, which was larger than that of age (0.571), gender (0.582), stage (0.703), and tumor family history (0.535) (*Figure 6A*). On the other hand, the AUC of 1-, 3-, and 5-year OS was 0.732, 0.705, and 0.778, respectively, which confirmed the favorable diagnostic significance of this prognostic model (*Figure 6B*). In addition, a C-index curve was also constructed to compare the consistency index of risk score with other clinical features (age, gender, stage, and tumor family history). It was revealed that the C-index value of the risk score was larger than that of other clinical features (*Figure 6C*), which verified the high prediction accuracy of this model.

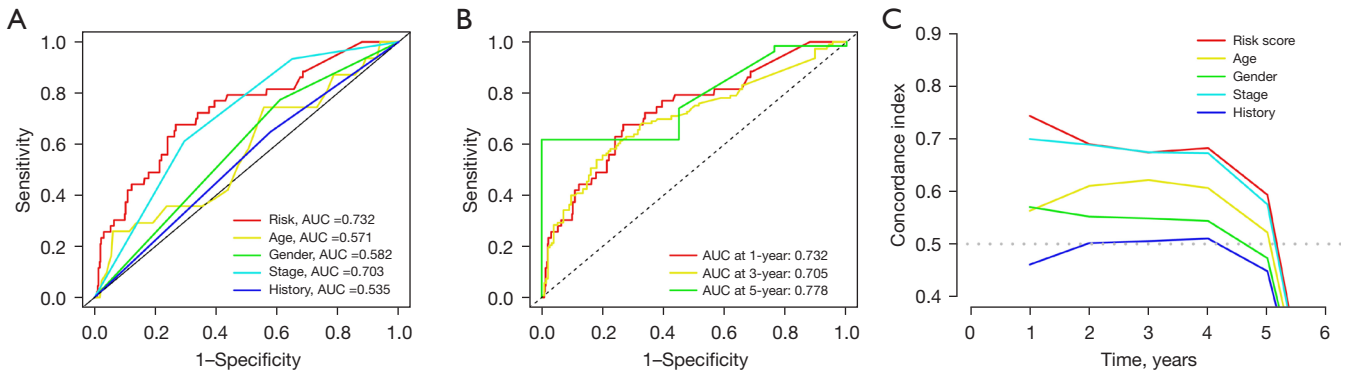

Figure 6 Evaluation of the accuracy of this prognostic model (A) ROC curve of clinical features, (B) ROC curve of the risk model for 1-, 3-, and 5-year OS, and (C) C-index curve. AUC, area under the curve; ROC, receiver operating characteristic; OS, overall survival.

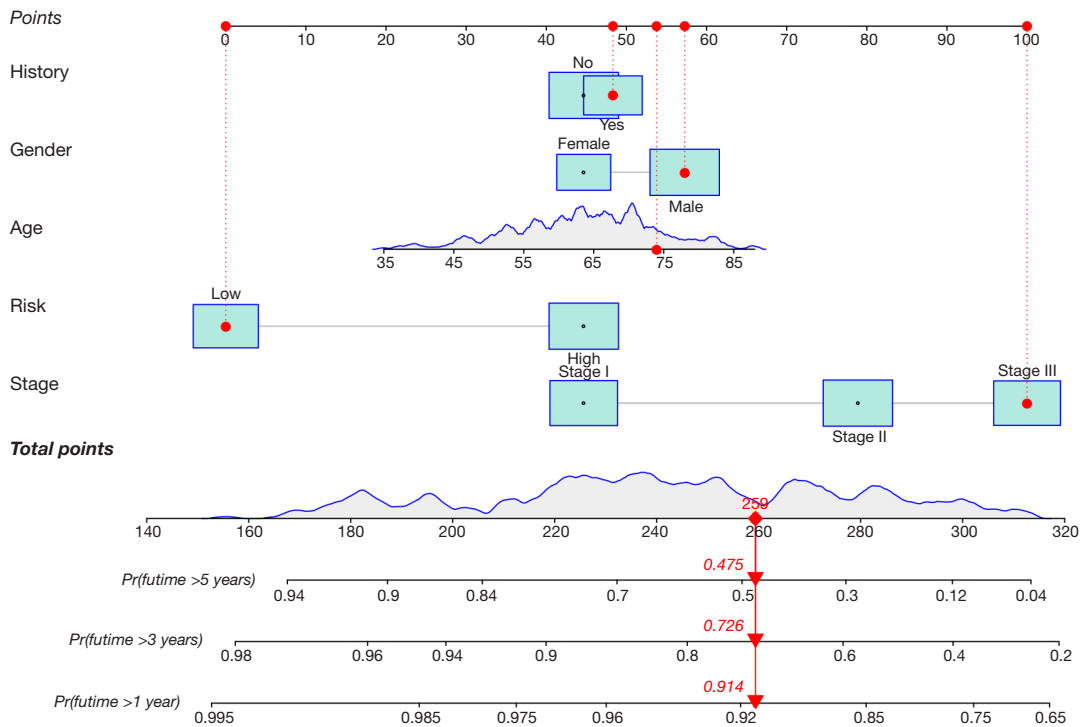

Figure 7 A nomogram based on the age, gender, stage, risk score, and tumor family history from the signature.

Construction of nomogram of clinical subgroups

Moreover, a nomogram was constructed based on the age, gender, ISS stage, risk score, and tumor family history from the signature (*Figure* 7) to predict the OS of patients. The total score calculation results demonstrated that the nomogram was effective in predicting the 1-, 3- and 5-year OS of MM patients. As the example shown in the *Figure* 7, the patient is a male and the age is 74 with a tumor family history. The risk score is low and the ISS stage is level 3. The total score calculation is 259, and the probability of living more than 1 year is 0.914. The probability of living more than 3 years is 0.726, while the probability of living more than 5 years is 0.475.

Differential risk analysis and functional enrichment analysis

The DERGs were extracted from the samples of the high-

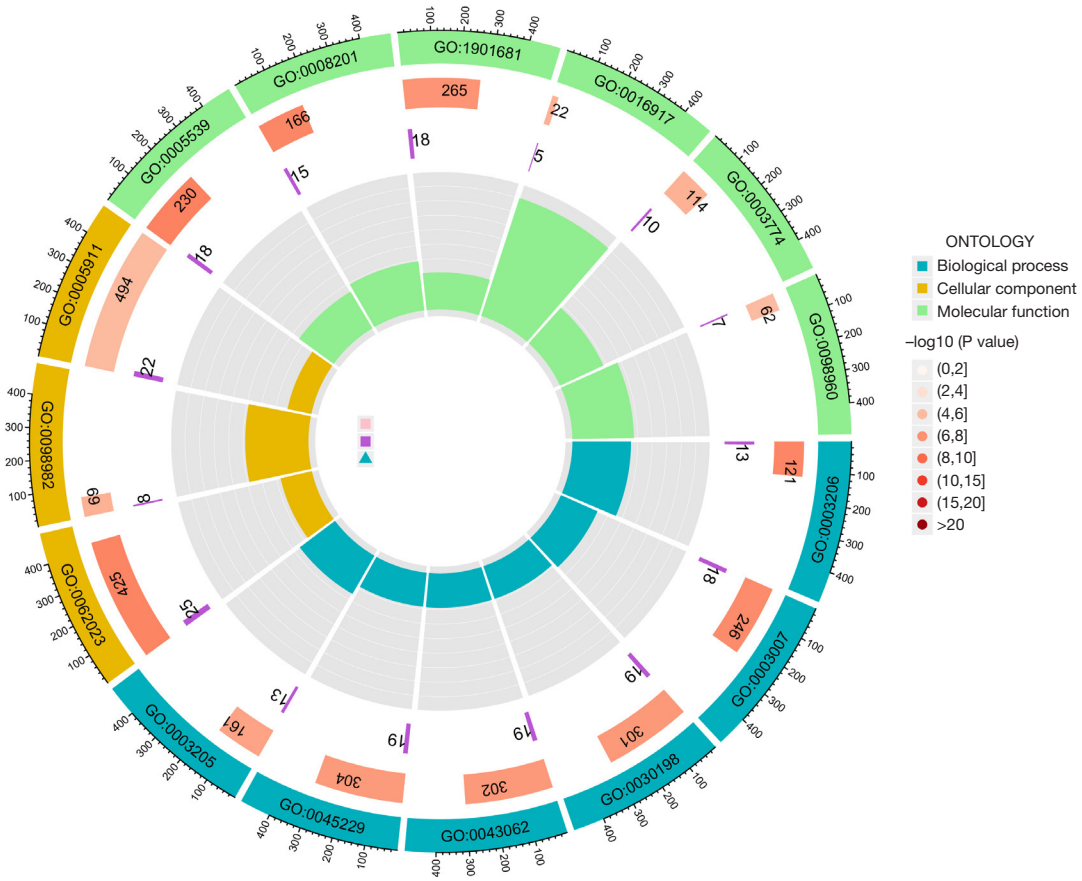

Figure 8 Results of GO analysis. GO, Gene Ontology.

and low-risk groups by the limma package in R software. The results demonstrated that there were significant differences in the expression of 581 genes in MM patients between the high- and low-risk groups ($|\log_2 FC| > 1$, $P<0.05$). The functional enrichment analysis was also performed on 581 DERGs. The GO analysis results showed that these DERGs were mainly concentrated on such ontology annotations as extracellular structure organization, collagen-containing extracellular matrix, glycosaminoglycan binding, and sulfur compound binding (*Figure 8*, *Table 2*). The KEGG analysis showed that the DERGs may be related to neuroactive ligand-receptor interaction and mitogen-activated protein kinase (MAPK) signaling pathway. This finding indicated that these DERGs may be involved in the progression of tumors (*Figure 9*).

Discussion

MM is the second most common hematological malignant tumor in adults, and its incidence is on the rise worldwide (39,40). Despite the advancement in the treatment of MM with the emergence of several new drugs (carfilzomib, pomalidomide, daratumumab, elotuzumab, panobinostat, ixazomib, and Selinexor), this cancer is still incurable in most patients (41). There is an urgent demand for identifying reliable prognostic biomarkers and new therapeutic targets for MM. In recent years, the contribution of lncRNAs to cancer progression has been widely recognized (42,43). Li (44) found that cuproptosis played an important role in hematological tumors. However, there are few studies on the co-regulatory role of cuproptosis and lncRNAs in MM. Hence, exploring the biomarkers related to the prognosis of MM may have a favorable prospect in clinical application. In this study, a prognostic risk model was established for MM patients with cuproptosis-related lncRNAs.

With the assistance of bioinformatics analysis, the bone marrow tissue transcriptome data of 575 MM patients and clinical data of 516 MM patients were screened from

Table 2 Specific number and name of Gene Ontology

Ontology	ID	Description	P.adjust	q value	Count
BP	GO: 0030198	Extracellular matrix organization	0.001479447	0.001330466	19
	GO: 0043062	Extracellular structure organization	0.001479447	0.001330466	19
	GO: 0045229	External encapsulating structure organization	0.001479447	0.001330466	19
	GO: 0003007	Heart morphogenesis	0.000714112	0.000642201	18
	GO: 0003206	Cardiac chamber morphogenesis	0.000714112	0.000642201	13
	GO: 0003205	Cardiac chamber development	0.003280404	0.002950066	13
CC	GO: 0062023	Collagen-containing extracellular matrix	6.91E–05	6.09E–05	25
	GO: 0005911	Cell-cell junction	0.009584801	0.008453167	22
	GO: 0098982	GABA-ergic synapse	0.005135118	0.004528838	8
MF	GO: 0005539	Glycosaminoglycan binding	6.63E–05	5.76E–05	18
	GO: 1901681	Sulfur compound binding	0.000203826	0.000177183	18
	GO: 0008201	Heparin binding	6.63E–05	5.76E–05	15
	GO: 0003774	Cytoskeletal motor activity	0.003421737	0.002974461	10
	GO: 0098960	Postsynaptic neurotransmitter receptor activity	0.00879237	0.007643065	7
	GO: 0016917	GABA receptor activity	0.003421737	0.002974461	5

BP, biological process; GO, Gene Ontology; CC, cellular component; MF, molecular function; GABA, gamma-aminobutyric acid.

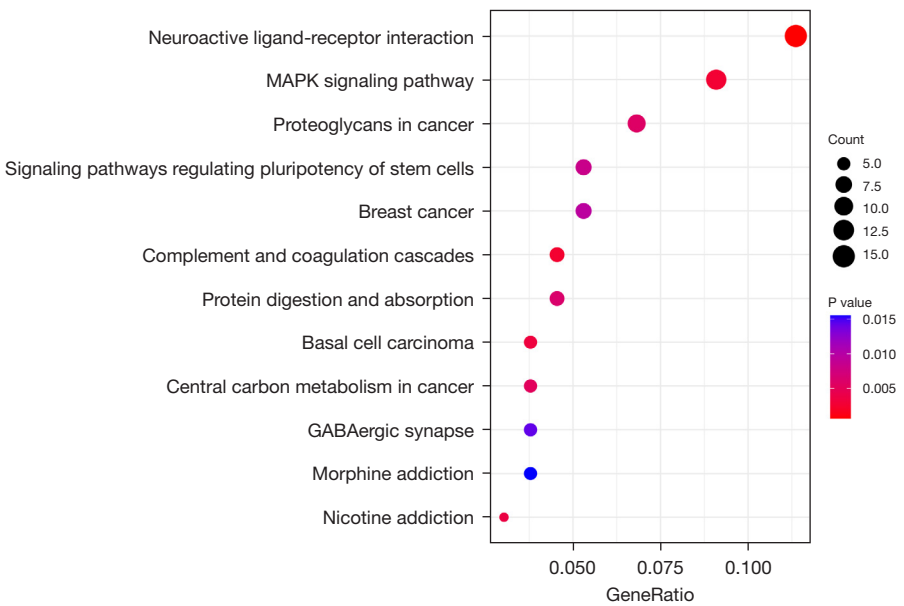

Figure 9 Results of KEGG analysis. KEGG, Kyoto Encyclopedia of Genes and Genomes; MAPK, mitogen-activated protein kinase; GABA, gamma-aminobutyric acid.

the TCGA database. After a series of cuproptosis-related genes were obtained from recent reports, cuproptosis-related lncRNAs were selected by the co-expression analysis of cuproptosis-related genes and lncRNAs. Then, 12 cuproptosis-related lncRNAs were screened by the LASSO Cox regression analysis, including AC105206, LINC00620, AL080284.1, AC013480.1, AL158198.1, TLX1NB, CNTFR-AS1, ATP6V1B1-AS, AC092435.1, AC022784.2, AP000428, and AL603824.1. Subsequently, a prognostic risk model was constructed for MM patients. The multivariate Cox regression analysis results showed that age, stage, and risk score were independently correlated with the OS of MM patients and hence could be used as independent prognostic biomarkers. Besides, the clinical data of MM patients were randomly divided into the training group and the testing group, and these patients were divided into the low- and high-risk groups based on the median risk score. The Kaplan-Meler survival analysis results showed that there was a significant difference in the survival rate between the high- and low-risk groups ($P<0.001$). In addition, the ROC curve and C-index curve analysis results proved the effectiveness of risk score as a prognostic biomarker. Finally, the difference risk analysis and function enrichment analysis were carried out among risk groups.

Among the 12 cuproptosis-related lncRNA genes associated with the prognosis of MM, TLX1NB and CNTFR-AS1 were verified to play a role in this cancer. TLX1NB is an overexpressed oncogene, and it is related to the tumor progression of lung cancer, colorectal cancer, and glioma. Duan *et al.* (45) found the low expression and hypermethylation of TLX1NB in patients with low-grade gliomas, and TLX1NB had a certain impact on the prognosis of low-grade gliomas. Further, they concluded that TLX1NB may be an early biomarker for the recurrence of low-grade gliomas. Chen *et al.* (46) found that the expression of TLX1NB was up-regulated in colon cancer tissue. They confirmed that TLX1NB can promote the invasion, migration, and metastasis of colon cancer cells by promoting the phosphorylation of STAT5A and it also played an important role in regulating cancer. Dastjerdi *et al.* (47) revealed that TLX1NB was overexpressed in colon cancer. It had potential carcinogenic characteristics and can be used as a diagnostic factor to detect tumors in normal samples. In a study of Li *et al.* (48), it was suggested that TLX1NB regulated CRISP1 through hsa-miR-148b-3p and can be considered a potential therapeutic target for lung adenocarcinoma. In addition, Li *et al.* (49) also found that the high expression of CNTFR-AS1 was related to the low survival rate of triple negative breast cancer, and it may be used as a potential biomarker for the treatment and prognostic classification of different breast cancer subtypes.

In order to clarify the potential regulatory mechanism among different risk groups, the functional enrichment analysis was performed on 581 DERGs. According to the GO analysis results, risk factors seemed to be closely related to the extracellular matrix, which was a key component in the tumor microenvironment for the regulation of cell growth and development and contributed to the transmission of cell signals. Therefore, it can be speculated that cuproptosis-related lncRNAs may play a key role in the tumor microenvironment of MM. The KEGG analysis results indicated that differentially expressed cuproptosis-related lncRNAs were highly enriched in the MAPK signaling pathway. There are five MAPK signaling pathways in mammals, which play an important role in tumor proliferation, apoptosis, invasion, and metastasis and participate in the occurrence and development of many kinds of tumors, including MM (50). It was demonstrated in a previous study that the activation of the MAPK pathway mediated the proliferation, survival, and migration of MM cells (51). Up to 50% of patients newly diagnosed with MM are affected by the abnormal MAPK pathway. Zhang *et al.* (52) found that inhibiting the MAPK pathway can reduce the proliferation and migration of colon cancer cells. In this study, the KEGG analysis results demonstrated that the differentially expressed cuproptosis-related lncRNAs were highly enriched in the signaling pathway of neuroactive ligand-receptor interaction. This indicated that cuproptosis-related lncRNAs may be involved in the signaling pathway of neuroactive ligand-receptor interaction. Neuroactive ligands have been verified to affect neuronal functions by binding intracellular receptors and can bind transcription factors and regulate gene expression (53,54).

To sum up, some bioinformatics methods combined with the TCGA database were adopted in this study to screen cuproptosis-related lncRNAs. The results demonstrated that TLX1NB and CNTFR-AS1 could regulate the prognosis of MM patients. Nevertheless, there are some limitations in this study. The related research on cuproptosis-related genes is still in the early stage, this paper only applied the cuproptosis-related genes reported at present, and more cuproptosis-related genes may be found in the future. There was a significant difference in gene expression between the high- and low-risk group. GO analysis showed that

risk characteristics were closely related to the extracellular matrix. The KEGG analysis results showed that cuproptosis-related lncRNAs were highly enriched in the MAPK pathway and neuroactive ligand-receptor interaction signaling pathway. In this study, however, relevant analyses were only performed from the perspective of statistics, and basic experiments were not conducted. The findings of this study provided an important basis and direction for follow-up basic experimental and clinical studies.

Conclusions

In this study, a novel cuproptosis-related lncRNA prognostic model was constructed for MM patients. TLX1NB and CNTFR-AS1 may be cuproptosis-related lncRNAs associated with the prognosis of MM patients. Besides, the differentially expressed risk genes between the high- and low-risk groups were also analyzed, and the GO and KEGG analyses were also carried out. These findings are anticipated to contribute to the improvement of clinical outcomes. However, further verification is still needed.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-960/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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