

Prognostic model based on autophagy-related lncRNAs in gastric cancer

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Abstract

Background: Gastric cancer (GC) is one of the most prevalent cancer in the world. Although increasing studies have indicated that autophagy-related long non-coding RNA (lncRNA) plays an essential role in the occurrence of GC, the prognosis of GC based on autophagy is still deficient.

Method: Autophagy-related lncRNAs were obtained by using the correlation test with the autophagy-related gene. Data was downloaded from The Cancer Genome of Atlas stomach adenocarcinoma (TCGA-STAD) dataset. The prognostic autophagy-related lncRNAs significantly correlated with survival of TCGA-STAD dataset were obtained by using Kaplan-Meier and univariate Cox regression analysis. TCGA-STAD dataset was separated into a training set and a testing set randomly. The model was constructed based on the training set through the least absolute shrinkage and selection operator (LASSO) regression. The testing set and TCGA-STAD were used to validate the accuracy of the model. Every patient got a risk score (RS) and patients were separate into high-risk group and low-risk group due to the median RS. The prognostic network was built and the mRNAs in the system were analyzed through Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis. The signaling pathways that the differentially expressed genes (DEGs) between two types of risk group mainly participated in were distinguished through Gene Set Enrichment Analysis (GSEA). The individual's survival rate was predicted through the nomogram.

Results: 24 autophagy-related lncRNAs were found strongly associated with the survival of the TCGA-STAD dataset. Among them, 11 lncRNAs were selected to build the risk score model through LASSO regression. The multivariate Cox analysis showed that the RS could be an independent prognosis predictor. The Kaplan-Meier survival analysis and the Receiver Operating Characteristic (ROC) curve indicated the model had an excellent prediction effect. GO, and KEGG analysis revealed that the mRNAs in the prognostic network were mainly involved in the autophagy and ubiquitin-like protein ligase binding. GSEA analysis uncovered that the DEGs in high-risk group partially participated in the ECM receptor interaction and other signaling pathways.

Conclusions: Our results indicated that the risk score model based on the autophagy-related lncRNAs performed well in the prediction of prognosis for patients with GC.

Background

Gastric cancer (GC) is the fifth most prevalent tumor and one of the deadliest carcinomas worldwide [1], among which 90% are adenocarcinomas [2]. Although there has been a stable decreasing in GC occurrence and mortality rates globally over several decades after the beginning of 19th century [3, 4], GC remains a high case fatality rate of 75% throughout the world [5]. Due to the insufficient understanding of the molecular mechanism [6] and the lack of relevant clinical prediction systems [7], most patients with GC have already been in the advanced stage when they are diagnosed [8], which brings great trouble to the patient's survival [9] and clinical therapy. Therefore, it is critical to construct an accuracy prediction

system for GC, which have the ability for early diagnosis and prevent the disease before premalignant lesions have developed.

Autophagy is a highly conserved and evolutionarily ancient catabolic process which can degrade the misfolded proteins and damaged organelles [10]. For the past few years, knowledge about the function of autophagy has developed. It has been found that autophagy participated in a plenty of physiological processes in mammal, including quality control of proteins and organelles, immunity, nutrient deprivation, hypoxia, drug stimuli, stress, and prevention of neurodegeneration [11]. Autophagy can also regulate biological process including apoptosis, protein synthesis, cell growth and proliferation through the AMPK/mTOR pathway, PI3K/Akt/mTOR pathway, P53 pathway and other signaling pathways [12–14]. What' more, the role of autophagy in the progression of carcinoma also has several breakthroughs.

The effect of autophagy is considered controversial in tumorigenesis, which can both promote and suppress cancer development under different cell types or stress modes [15]. In general, it is thought that autophagy prevented carcinogenesis [16, 17]. Nevertheless, once tumor is established, increased autophagic flux often promotes tumor cell growth by providing energy and vital compounds upon various stress stimuli [18]. Similarly, growing studies have also proved that autophagy had a significant effect on the GC.

The role of autophagy in GC is also complex and contradictory. Some researches supported that the autophagy was a tumor promoter in GC. Cause autophagy inhibitor will destroy the protective mechanism of GC cell and promotes cell death induced by therapeutic drugs [19–21]. However, PD-L1 expression was also found enhanced by autophagy inhibition in GC [22]. What's more, a study has shown that autophagy inducers such as AMPK inducers could be used in the GC treatment, which will lead to autophagic cell death of tumor cells [23].

In recent years, the relationship between long non-coding RNA (lncRNA) and autophagy has several breaks in the diagnosis, treatment, and prognosis of GC. Pieces of evidence showed that lncRNA is vital for the occurrence, prognosis, and chemoresistance of GC by regulating autophagy-related mRNA [24–26]. Some studies have demonstrated that silencing of LINC01419 and CCAT2 promotes autophagy through constraining the PI3K/Akt1/mTOR pathway thus inhibiting the invasion and migration of GC cells [27, 28]; Another study also revealed that autophagy was associated with the proliferation of GC cells, partially due to the MALAT1 promoted by downregulating miR-204 [29]. However, most of these experiments only explored the role of one or a few lncRNAs in the autophagy of GC, and could not fully explain the relevant mechanisms.

To be concluded, the role of autophagy-related lncRNA in GC is complicated and controversial, which involves hundreds of molecular in this process. Therefore, a model consisted of multiple autophagy-related lncRNAs will have a better prognosis predicting accuracy than the single. For this purpose, we built a risk score model based on the multiple autophagy-related lncRNAs, which also performed well in the prediction of prognosis for the GC patients in the clinic.

Materials And Methods

Screening for the autophagy-associated lncRNAs

Autophagy-associated genes were obtained through the HADb: Human Autophagy Database website (<http://www.autophagy.lu/>). Autophagy-related lncRNAs were obtained by using the correlation test of these genes with R version 3.6.3 software (Pearson correlation coefficient > 0.3, $P < 0.001$).

Data acquisition

All 350 patients' data of STAD were downloaded from The Cancer Genome Atlas (TCGA) website (<https://portal.gdc.cancer.gov/>). All the data was submitted to R software and randomly separated into the training set and testing set.

Identification of the prognostic autophagy-related lncRNAs

Kaplan-Meier and univariate Cox regression analysis was applied to select the prognostic autophagy-related lncRNA in TCGA-STAD dataset ($P < 0.05$).

Survival analysis

Least absolute shrinkage and selection operator (LASSO) regression was adopted to build the model using the R package "glmnet" with prognostic autophagy-related lncRNAs selected before. In this process, only the most potent prognostic markers were chosen and constituted the optimal panel of prognosis which achieved the best performance. Each patient got a risk score (RS) incorporating the expression of the lncRNAs (Exp_i) and the corresponding LASSO coefficients ($Coef_i$), $Risk\ Score = \sum_{i=1}^n Exp_i * Coef_i$. The median RS was chosen to divide patients into high-risk group and low-risk group in the training set, testing set and TCGA-STAD dataset respectively. Multivariate Cox regression was used to assess whether the RS could be an independent predictor. Kaplan-Meier curves were used to check the significant difference in survival probability for patients between two types of risk group. An area under the Receiver Operating Characteristic (ROC) curve (AUC) was used to examine the accuracy. All statistics were processed through R version 3.6.3 software (<https://www.r-project.org/>) ($P < 0.05$).

Network construction and pathway analysis

The co-expressed mRNAs were obtained by using the correlation test with R software (Pearson correlation coefficient > 0.3, $P < 0.001$). The network was constructed and visualized through Cytoscape software (<https://cytoscape.org/>). The Sankey diagram was built using the R software. The Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis were performed using the "clusterProfiler" package of R software (Gene ratio > 0.05, $P < 0.05$). The signaling pathways that the differentially expressed genes (DEGs) mainly participated in between two types of risk group were distinguished through Gene Set Enrichment Analysis (GSEA).

A nomogram was constructed through the “rms” package for R combining the risk type and other clinical features including age, gender, stage, and TNM stage to predict the individual’s survival probability.

Results

Characteristics of patients

TCGA-STAD dataset was patients diagnosed with stomach adenocarcinoma, which consisted of a total of 350 patients. Kaplan-Meier survival curves were plotted for TCGA-STAD dataset regarding major clinical features (Supplementary Fig).

Selecting of prognostic autophagy-related LncRNA for TCGA-STAD dataset

The autophagy-related lncRNAs were obtained by using the correlation test of autophagy-related genes (Pearson correlation coefficient > 0.3 , $P < 0.001$). A total of 24 autophagy-related lncRNAs were significantly correlated with the survival for TCGA-STAD through Kaplan-Meier and univariate Cox regression analysis ($P < 0.05$) (Fig. 1).

Construction of prognostic risk score model based on autophagy-related lncRNAs

All the patients from TCGA -STAD cohort were randomly separated into a training set and testing set ($P > 0.05$) (Table 1). Then all these 24 identified prognostic lncRNAs were analyzed with the LASSO regression analysis (Fig. 2a) and 3-fold positive cross-validation (Fig. 2b) in the training set. The regression coefficient was computed to select the optimal panel of prognosis. The model achieved the best performance while 11 autophagy-related lncRNAs were included. Combining the expression of the autophagy-related lncRNAs and LASSO coefficients (Table 2), each patient got a RS as a measure of survival risk.

Table 1
Major clinical characteristics for the STAD patients in the training set, testing set and TCGA-STAD dataset

Characteristics	TCGA-STAD cohort		P value
	Training set n = 175(%)	Testing set n = 175(%)	
Age			0.1918
30–50	19(10.86%)	10(5.71%)	
50–70	104(59.43%)	96(54.86%)	
70–90	52(29.71%)	69(39.43%)	
Gender			0.3265
female	62(35.43%)	62(35.43%)	
male	113(64.57%)	113(64.57%)	
T stage			0.909
T1-T2	37(21.14%)	53(30.29%)	
T3-T4	138(78.86%)	122(69.71%)	
N stage			
N1	49(28.00%)	54(30.86%)	0.6206
N2	44(25.14%)	49(28.00%)	
N3	35(20.00%)	37(21.14%)	
N4	47(26.86%)	35(20.00%)	
M stage			
M0	156(89.14%)	154(88.00%)	0.2374
M1	19(10.86%)	21(12.00%)	
Clinical Stage			0.6475
Stage I	21(12.00%)	26(14.86%)	
Stage II	50(28.57%)	61(34.86%)	
Stage III	83(47.43%)	63(36.00%)	
Stage IV	21(12.00%)	25(14.29%)	
Pathological Grade			0.3813

Characteristics	TCGA-STAD cohort		P value
	Training set n = 175(%)	Testing set n = 175(%)	
Grade 1	4(2.29%)	5(2.86%)	
Grade 2	54(30.86%)	71(40.57%)	
Grade 3	117(66.86%)	99(56.57%)	
No significant differences. * $P > 0.05$			

Table 2

The lncRNAs in the risk score model were strongly associated with the survival in TCGA-STAD dataset

lncRNA	Kaplan-Meier analysis			Univariate Cox regression analysis				LASSO coefficient
	B	SE	P-value*	HR	HR.95L	HR.95H	P-value*	
AC092574.1	-0.348	0.171	0.006	0.706	0.505	0.987	0.042	-0.009
AL353804.1	-0.279	0.131	0.002	0.757	0.585	0.979	0.034	-0.238
AC005586.1	-0.270	0.085	0.000	0.764	0.646	0.903	0.002	-0.178
IPO5P1	-0.223	0.092	0.022	0.800	0.668	0.959	0.016	-0.171
AL355574.1	-0.207	0.076	0.033	0.813	0.701	0.943	0.006	-0.087
AP003392.1	-0.187	0.092	0.017	0.830	0.692	0.994	0.043	-0.052
HAGLR	0.081	0.030	0.001	1.084	1.023	1.149	0.007	0.065
LINC01705	0.092	0.041	0.039	1.097	1.012	1.188	0.024	0.027
AP001033.2	0.195	0.099	0.049	1.215	1.000	1.477	0.050	0.154
AC009948.1	0.197	0.079	0.041	1.218	1.043	1.423	0.013	0.252
AP001528.2	0.346	0.130	0.026	1.413	1.095	1.825	0.008	0.065
HR, hazard ratio; HR.95L-HR.95H, 95% confidential interval. * $P < 0.05$								

Validation of the risk score model for survival prediction in the training set, testing set and TCGA-STAD dataset

Based on the median RS, patients were divided into high-risk group and low-risk group. lncRNA *AC005586.1*, *AL353804.1*, *IPO5P1*, *AP003392.1*, *AL355574.1* and *AC092574.1* were considered as protective lncRNA (HR < 1, B < 0, LASSO coefficient < 0) while *LINC01705*, *AP001528.2*, *AC009948.1*, *HAGLR* and *AP001033.2* were risk lncRNA (HR > 1, B > 0, LASSO coefficient > 0). The heatmap showed the

Loading [MathJax]/jax/output/CommonHTML/fonts/TeX/fontdata.js group in training set (Fig. 3a), testing set

(Fig. 3b) and TCGA-STAD dataset (Fig. 3c). As illustrated, the low-risk group tended to express protective lncRNA while the high-risk group were more likely to express risk lncRNA. The correlation between RS and survival time and status in STAD patients were also plotted in the training set (Fig. 3e), testing set (Fig. 3f) and TCGA-STAD dataset (Fig. 3g). In all these datasets, patients with higher RS tended to face a shorter survival time and worse survival status.

Multivariate Cox regression analysis was used to evaluate the independent prognostic indicators. The results of the multivariable analysis showed the RS was a robust and independent prognostic indicator in the training set (Fig. 4a), testing set (Fig. 4b) and TCGA-STAD dataset (Fig. 4c) ($P < 0.05$). Kaplan-Meier analysis was also conducted on the training set (Fig. 4d), testing set (Fig. 4e) and TCGA-STAD dataset (Fig. 4f). Distinctly, there is a strong and significant difference between the two types of risk groups ($P < 0.0005$). Furthermore, ROC curve was adopted to appraise the accuracy of the model in the training set (Fig. 4g), testing set (Fig. 4h) and TCGA-STAD dataset (Fig. 4i). The area under the curve (AUC) was applied to evaluate the accuracy of the model's prediction in 1-year, 3-year, and 5-year. The value of AUC prompts the model to predict well in prognostic prediction.

Construction of the prognostic mRNA-LncRNA network and identification of involved signaling pathways

The mRNAs co-expressed with the lncRNAs in the risk score model were obtained by using the correlation test with R (Pearson correlation coefficient > 0.3 , $P < 0.001$). Then all these mRNAs and lncRNAs were used to construct the prognostic mRNA-lncRNA interaction network (Fig. 5a and Fig. 5b). The most significant GO terms for biological process (BP) (Fig. 5c), cellular component (CC) (Fig. 5d), and molecular function (MF) (Fig. 5e), as well as KEGG pathways (Fig. 5f), were analyzed to reveal potential biological functions of the mRNAs in the network (Gene ratio > 0.05 , $P < 0.05$). The results showed that the mRNAs in the network were mainly involved in autophagy both in GO and KEGG analysis. GSEA analysis uncovered that the DEGs were significantly enriched in several common signaling pathways (Fig. 5g) (Table 3).

Table 3
The results of the GSEA analysis

Signaling pathway	NES	NOM <i>p</i> -value*	FDR <i>q</i> -value*
ECM receptor interaction	2.05	0.00	0.05
Neuroactive ligand receptor interaction	2.02	0.00	0.03
Complement and coagulation cascades	1.97	0.00	0.04
Focal adhesion	1.89	0.01	0.04
Calcium signaling pathway	1.88	0.00	0.04
Peroxisome	-2.26	0.00	0.00
Base excision repair	-2.19	0.00	0.00
Spliceosome	-2.15	0.00	0.00
Nucleotide excision repair	-2.11	0.00	0.01
RNA degradation	-2.11	0.00	0.01

NES: normalized enrichment score; FDR *q*-value: false discovery rate *q* value; NOM *p*-value: normalized *p* value; *FDR *q*-value < 0.05; *NOM *p*-value < 0.05.

Nomograms for personalized prognostic prediction in STAD patients

A nomogram incorporating the risk type and clinical characters was built to estimate individual survival probability quantitatively of STAD patients. The plot showed the 1-year, 3-year, and 5-year survival probabilities in TCGA-STAD dataset (Fig. 6).

Discussion

Autophagy is a self-degradative process that plays an essential role in equilibrating energy, eliminating misfolded or aggregated proteins, and reacting to stimuli [30]. To date, three types of autophagy have been found: macroautophagy, microautophagy and chaperone-mediated autophagy [11].

Macroautophagy is considered as the main form of autophagy, which is extensively studied compared to the other two types [31–33]. The process of autophagy is also classified into four critical steps: initiation, nucleation, maturation, and degradation [34]. In the past decades, researchers have discovered 32 autophagy-related genes (Atgs) in yeast, most of which are also highly conserved in mammals significantly [35].

In recent years, some researches have reported that autophagy has a strong relationship between the

Loading [MathJax]/jax/output/CommonHTML/fonts/TeX/fontdata.js clin1 (protein homologue of the yeast ATG6)

was much overexpressed in malignant tissues than the nonmalignant tissues in GC. What's more, they also found that overexpression of Beclin1 was related with a poor prognosis for GC. Liao et al. [37] discovered that "stone-like" structure pattern of LC3A (an autophagosomal biomarker) was correlated with increased recurrence and worse survival possibility in gastric carcinoma.

As being recognized previously, lncRNAs such as H19 and HOTAIR played a key role as primary regulators in carcinogenesis of GC [38–40]. Until now, numerous studies have proved that lncRNAs were highly active in plenty of pathological processes of GC, such as proliferation and metastasis. Among them, some lncRNAs were defined as protective factors while others were risk factors [25, 41–44]. Furthermore, several studies have proved that lncRNAs participated in the progression, especially malignant progression of GC through regulating autophagy-related mRNAs [24–29, 45].

Although numerous researches have been performed and much is known about lncRNAs and autophagy in GC, previous studies mainly focused on the single lncRNA. The prognostic system relied on the multiple autophagy-related lncRNAs is still not clear. More importantly, as one of the deadliest cancers all over the world, prognosis evaluation of patients with GC still depend too much on the pathological analysis currently, which also facing many challenges and inconvenience in the clinic.

In this study, we obtained the autophagy-related lncRNAs through correlation test of the autophagy-related genes. The expression of the lncRNAs was profiled from the TCGA-STAD dataset. 24 lncRNAs were found strongly linked with the survival of TCGA-STAD through Kaplan-Meier and univariate Cox regression analysis. We used the LASSO regression analysis to build the model in the training set and found 11 prognostic signatures of lncRNAs. The RS was calculated by integrating lncRNAs expression levels and corresponding LASSO coefficients for each patient. *AC005586.1*, *AL353804.1*, *IPO5P1*, *AP003392.1*, *AL355574.1* and *AC092574.1* were considered as protective lncRNA while *LINC01705*, *AP001528.2*, *AC009948.1*, *HAGLR* and *AP001033.2* were risk lncRNA. The accuracy of the model was tested in the testing set, and TCGA-STAD dataset and the RS was found significantly corresponded with patient outcomes in both testing set and TCGA-STAD dataset.

GO analysis revealed that the mRNAs in the prognostic network were mainly involved in the autophagy, which is consistent with the expected results. The MF of GO analysis uncovered that these mRNAs were also have a link with ubiquitin or ubiquitin-like protein ligase binding. Ubiquitin (Ub) is a protein highly conserved in all eukaryotes and bears many potential sites for additional post-translational modifications [46]. Ub was one of the most prominent factors in modifying protein substrates and degradation [47]. The proteolytic system based on ubiquitin and autophagy are two prime systems in eukaryotic cells [48, 49]. Studies have shown that ubiquitin, as a capital regulator, has participated in all processes in the autophagy flux [50]. Atg8 was a ubiquitin-like protein, which was also found crucial for the autophagosome formation and consisted the lipid conjugation system in autophagy [51].

KEGG analysis uncovered that the mRNAs were primarily involved in the apoptosis, mTOR pathway, p53 pathway and PI3K-Akt pathway. There are two types of autophagy-related signaling pathways. One is Loading [MathJax]/jax/output/CommonHTML/fonts/TeX/fontdata.js and PI3K/Akt/mTOR pathways, and the other is

non-mTOR dependent pathways, such as the p53 pathway [52]. The PI3K/AKT/mTOR pathway regulates many biological processes, including autophagy and is frequently activated in various human cancers [53]. The molecular changes in the PI3K/Akt/mTOR signaling pathway were also found could increase the clinical stage and promote the recurrence in carcinoma [53, 54]. In GC, PI3K/Akt/mTOR activation was found significantly upregulated in GC cells, which results in the inhibition of autophagy of GC cells [55]. Additionally, inhibition of the PI3K/Akt/mTOR pathway increased the autophagic flux and promoted the apoptosis of cancer cells [56].

The results of the GSEA analysis showed that the high-risk group was much active in the ECM receptor interaction. Some studies indicated that autophagy affected the extracellular matrix (ECM), thus participating the invasiveness and metastasis of cancer cells. In a rapidly growing and aggressive tumor, biosynthesis is highly demanded obviously. And in this process, detachment-induced autophagy will help the cancer cells get rid of ECM contact and promoting the metastasis subsequently during advanced cancer stage [57, 58]. Autophagy will also induce metastatic cancer cells to hibernation if steady connection wasn't established between the new ECM microenvironment and the cancer cells [59, 60].

At last, we constructed a nomogram combining the risk type and other clinical features including age, gender, stage and TNM stage, which can predict an individual's clinical outcome quantitatively. By using the nomogram, every patient will get total points based on his or her various indicators respectively. The total points will predict the patient's survival probability in 1, 3-, and 5-year. Obviously, the higher the total points are, the lower the survival probability is.

Conclusion

In conclusion, we identified a prognostic risk score model consisted of 11 autophagy-related lncRNAs based on TCGA-STAD dataset. This model was an independent predictor and performed well for prognosis in the training set, testing set and TCGA-STAD dataset. A nomogram incorporating the model and clinical feature could accurately predict survival rate for individual GC patients. Our finding suggests that the 11-autophagy lncRNA risk score model may help facilitate individual prediction of patient's prognosis with GC in the clinic.

Abbreviations

AUC: area under the curve; BP: biological process; CC: cellular component; ECM: extracellular matrix; DEGs: differentially expressed genes; GC: gastric cancer; GO: Gene Ontology; GSEA: Gene Set Enrichment Analysis; HR: hazard ratio; KEGG: Kyoto Encyclopedia of Genes and Genomes; LASSO: least absolute shrinkage and selection operator; lncRNA: long non-coding RNA; MF: molecular function; ROC: Receiver Operating Characteristic; RS: risk score; STAD: stomach adenocarcinoma; TCGA: The Cancer Genome Atlas.

Declarations

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Authors' contributions

CMQ designed the risk score model; CMQ, CW and CB analyzed data; CMQ and CW wrote the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

No ethics involved.

Consent for publication

Written consent was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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Supplementary Figure Legend

Supplementary Fig Kaplan-Meier survival curves for TCGA-STAD dataset. Kaplan-Meier survival analysis regarding prime clinical features in GC. * $P < 0.05$

Figures

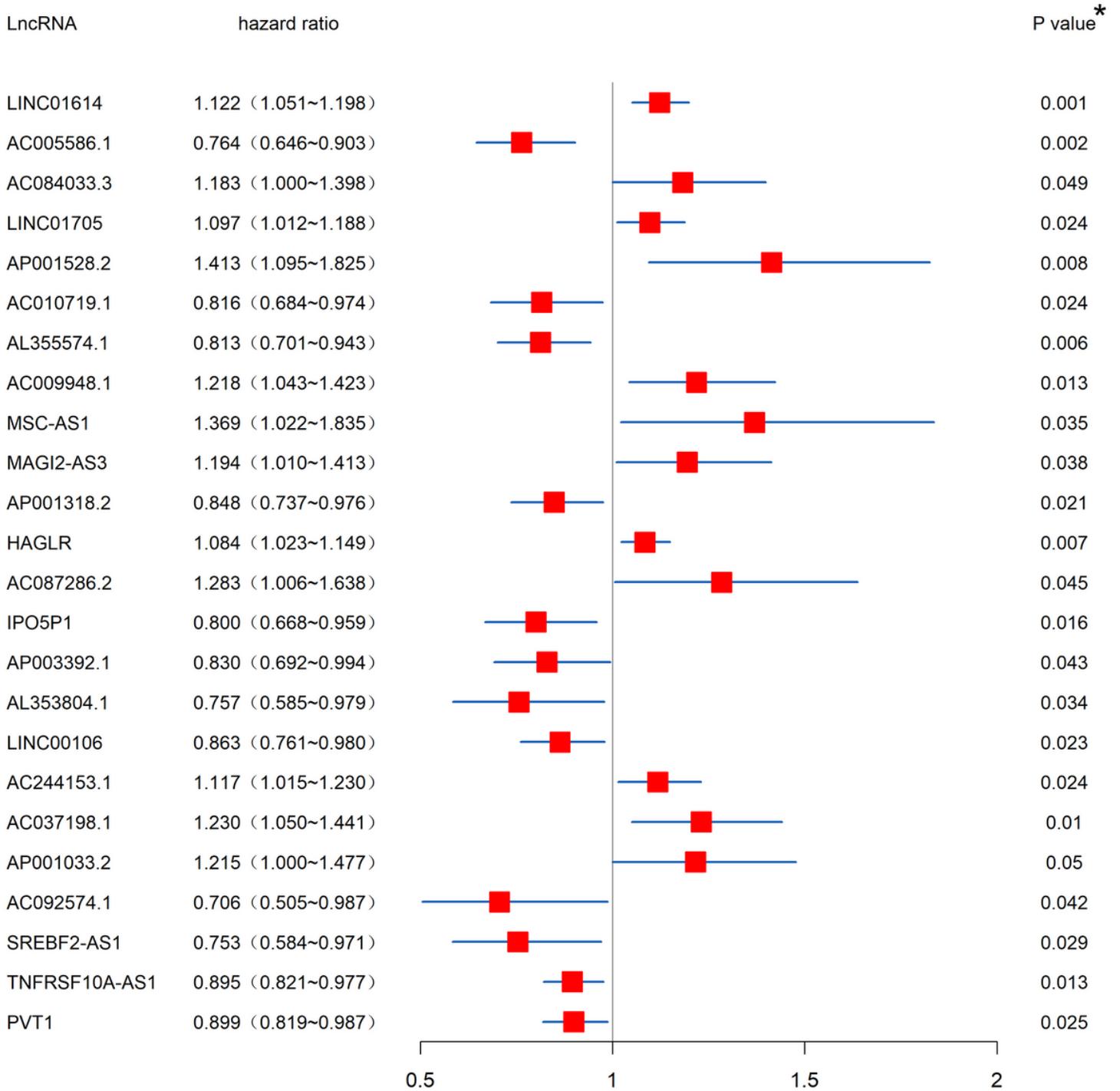


Figure 1

Screening of the autophagy-related lncRNAs linked with the survival in GC. Forest plot of prognostic autophagy-related lncRNAs in TCGA-STAD dataset based on Kaplan-Meier and univariate Cox regression analysis. *P < 0.05

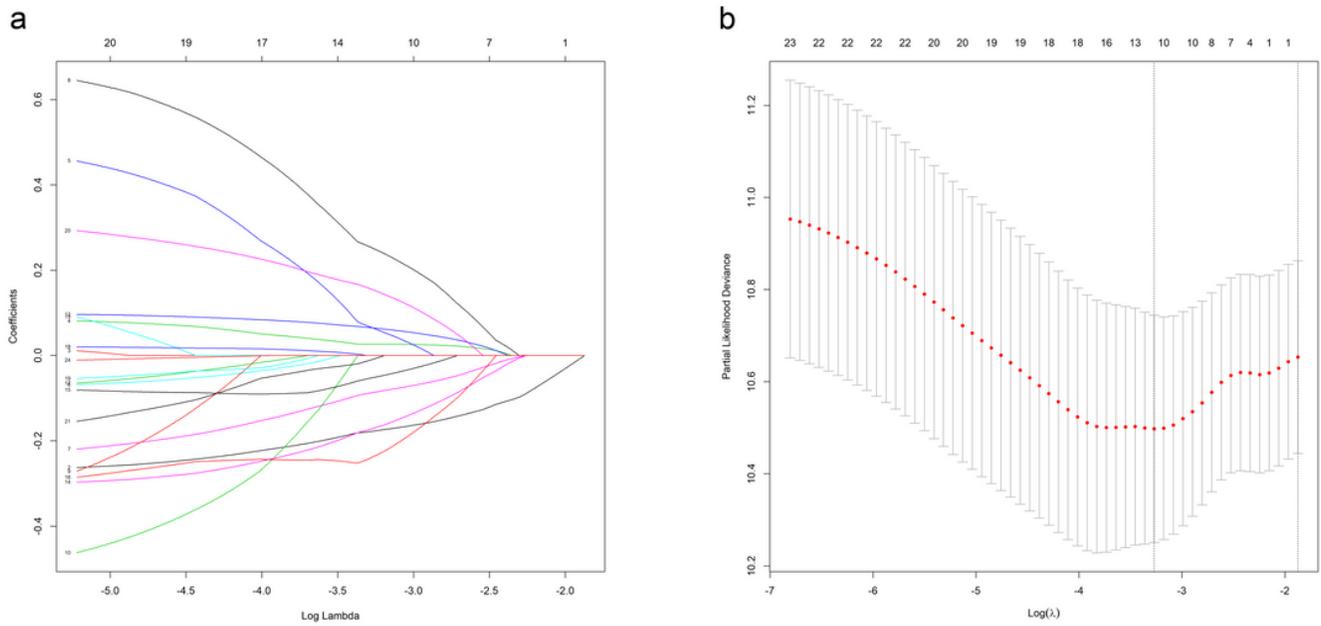


Figure 2

Construction of prognostic risk score model based on LASSO regression analysis. a Coefficient profile of each 24 prognostic autophagy-related lncRNA in the training set. b Selection of the optimal panel (lambda) for the model in the training set.

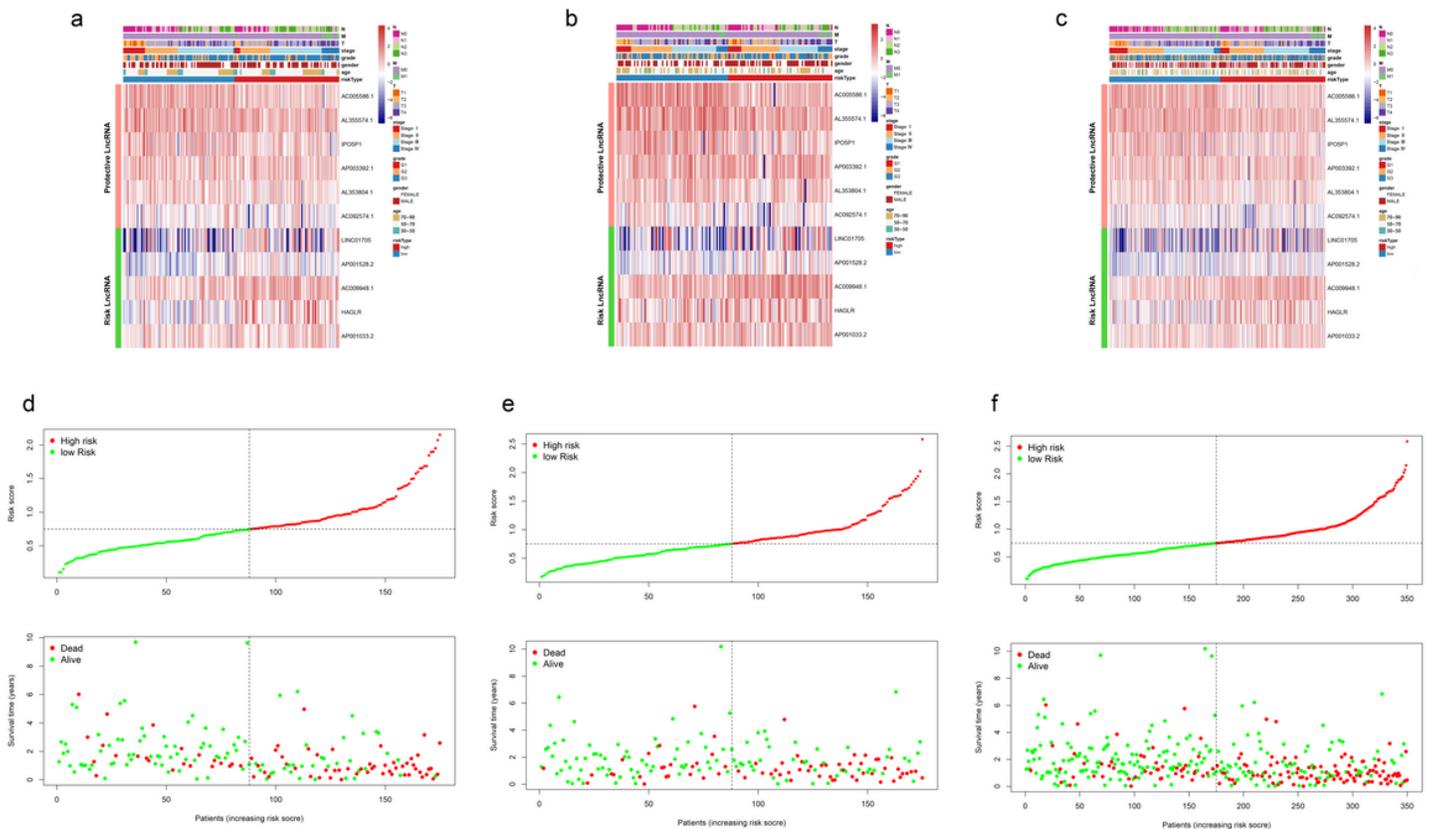


Figure 3

The link between clinical data and risk score a-c Heatmap plot for the lncRNAs in the model in the training set, testing set and TCGA-STAD dataset. d-e The relationship between the RS and survival time as well as status in the training set, testing set and TCGA-STAD dataset.

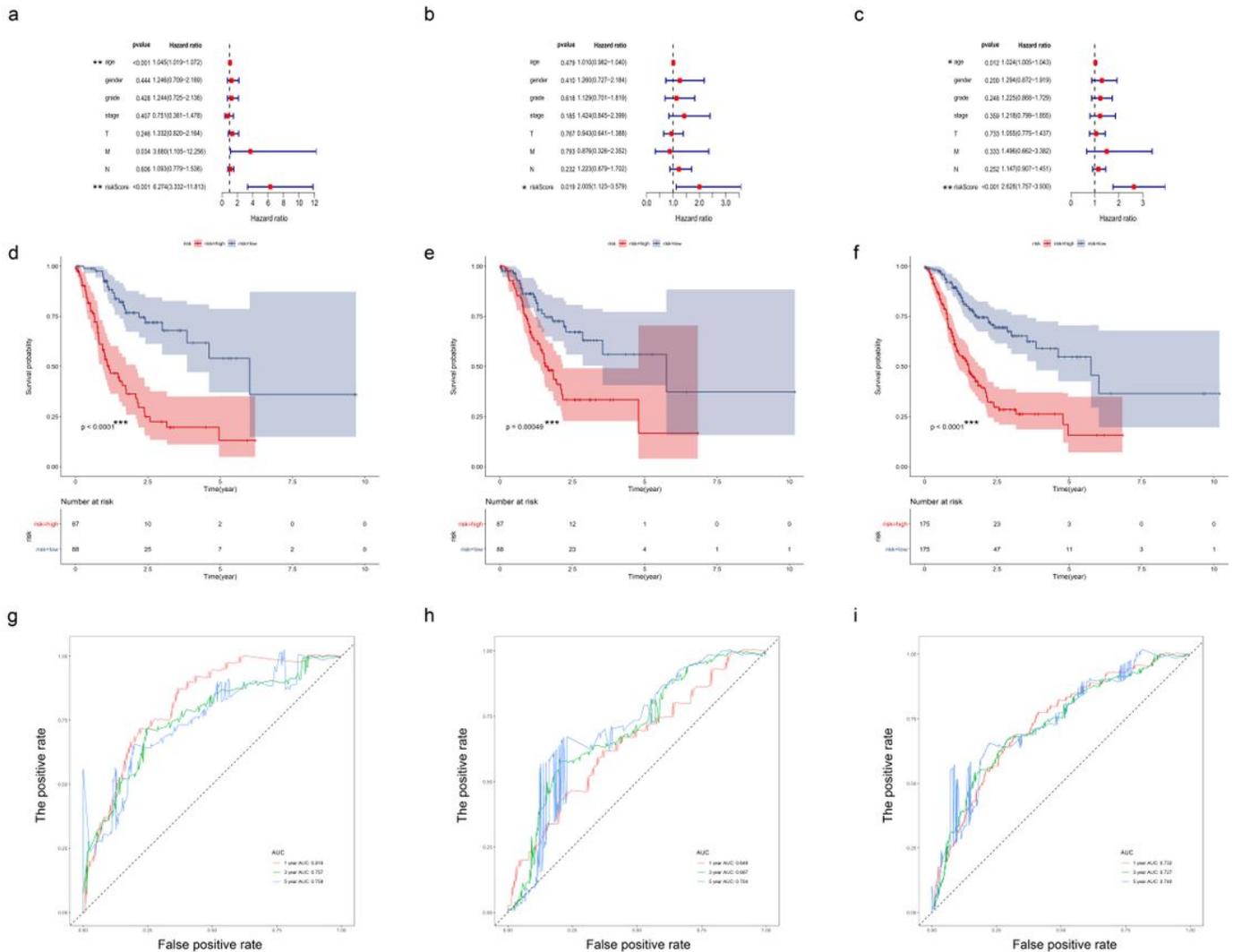


Figure 4

The risk score model performed well for survival prediction. a-c The RS was an independent prognostic predictor in the training set, testing set and TCGA-STAD dataset. d-f Kaplan-Meier analysis based on risk type in the training set, testing set and TCGA-STAD dataset. g-i The ROC curve and the value of AUC in 1-year, 3-year, and 5-year in the training set, testing set and TCGA-STAD dataset. *P < 0.05, **P < 0.001, ***P < 0.0005

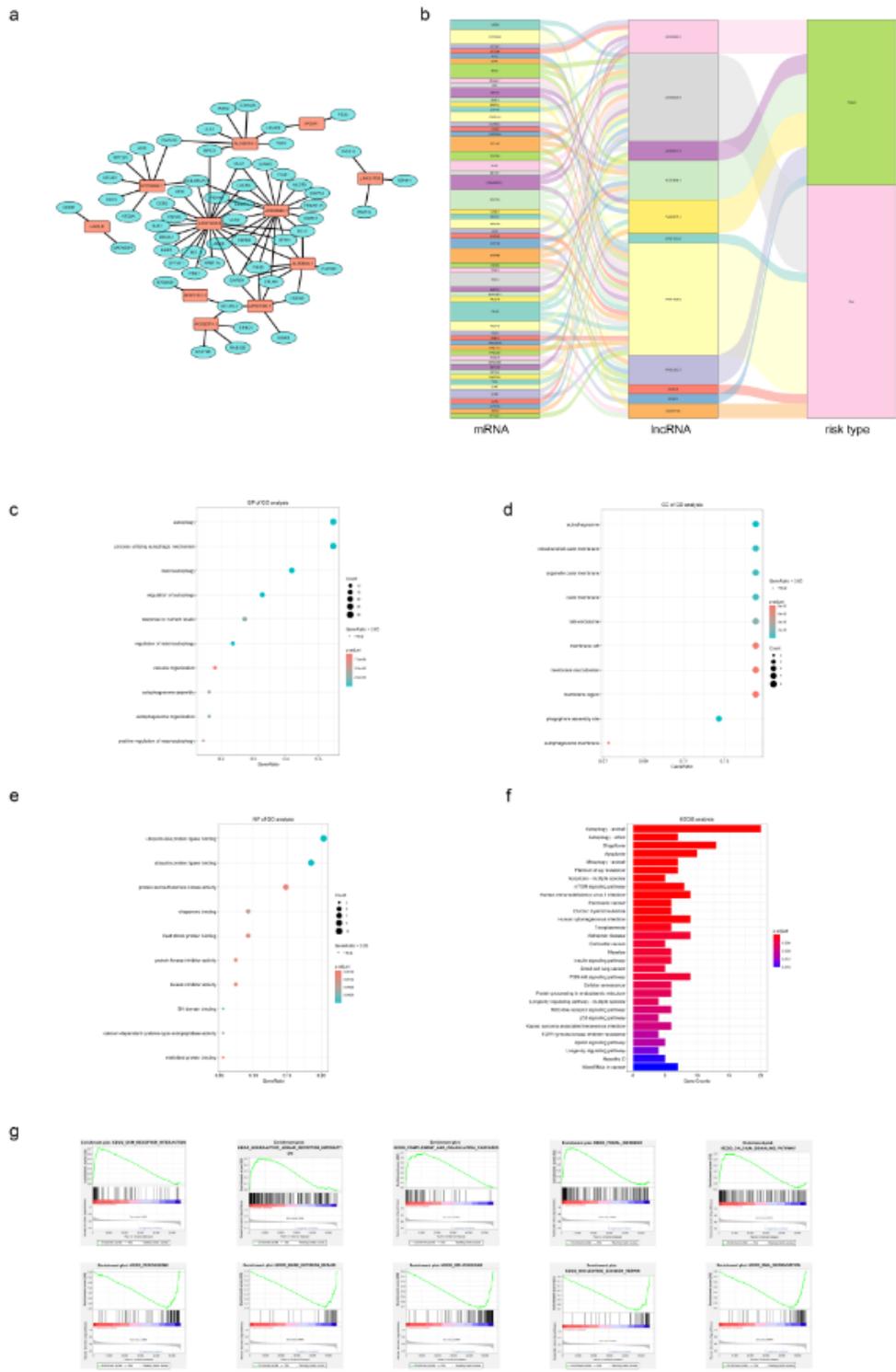


Figure 5

Construction of the prognostic mRNA-LncRNA interaction network and identification of involved signaling pathways. a The prognostic network based on the lncRNAs in the risk score model and the co-expressed mRNAs. b The Sankey diagram based on the prognostic network. c-e BP, CC, and MF of GO analysis for the mRNAs in the network. f KEGG analysis of the mRNAs in the network. g GSEA analysis of the DEGs

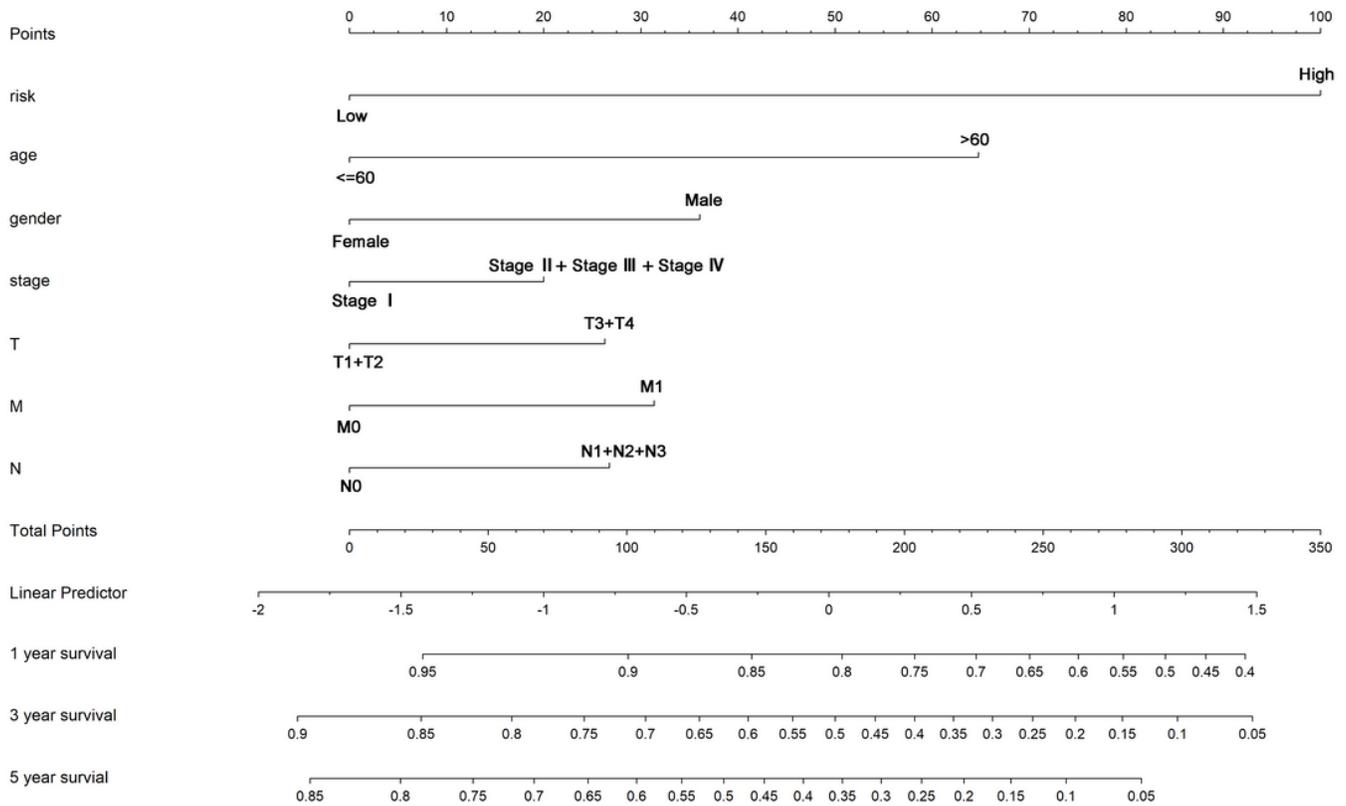


Figure 6

The nomogram for predicting an individual's survival rates in TCGA-STAD dataset. The nomogram is incorporated with the risk type and clinical features to predict personalized survival probabilities in 1-year, 3-year, and 5-year.

Supplementary Files

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