

Table S1 Summary of recognized angiogenesis-associated genes

Gene	Type
<i>POSTN</i>	Angiogenesis
<i>FSTL1</i>	Angiogenesis
<i>LRPAP1</i>	Angiogenesis
<i>STC1</i>	Angiogenesis
<i>LPL</i>	Angiogenesis
<i>VEGFA</i>	Angiogenesis
<i>PF4</i>	Angiogenesis
<i>THBD</i>	Angiogenesis
<i>FGFR1</i>	Angiogenesis
<i>TNFRSF21</i>	Angiogenesis
<i>CCND2</i>	Angiogenesis
<i>COL5A2</i>	Angiogenesis
<i>ITGAV</i>	Angiogenesis
<i>SERPINA5</i>	Angiogenesis
<i>KCNJ8</i>	Angiogenesis
<i>APP</i>	Angiogenesis
<i>JAG1</i>	Angiogenesis
<i>COL3A1</i>	Angiogenesis
<i>SPP1</i>	Angiogenesis
<i>NRP1</i>	Angiogenesis
<i>OLR1</i>	Angiogenesis
<i>PDGFA</i>	Angiogenesis
<i>PTK2</i>	Angiogenesis
<i>SLCO2A1</i>	Angiogenesis
<i>PGLYRP1</i>	Angiogenesis
<i>VAV2</i>	Angiogenesis
<i>S100A4</i>	Angiogenesis
<i>MSX1</i>	Angiogenesis
<i>TIMP1</i>	Angiogenesis
<i>APOH</i>	Angiogenesis
<i>PRG2</i>	Angiogenesis
<i>JAG2</i>	Angiogenesis
<i>LUM</i>	Angiogenesis
<i>CXCL6</i>	Angiogenesis

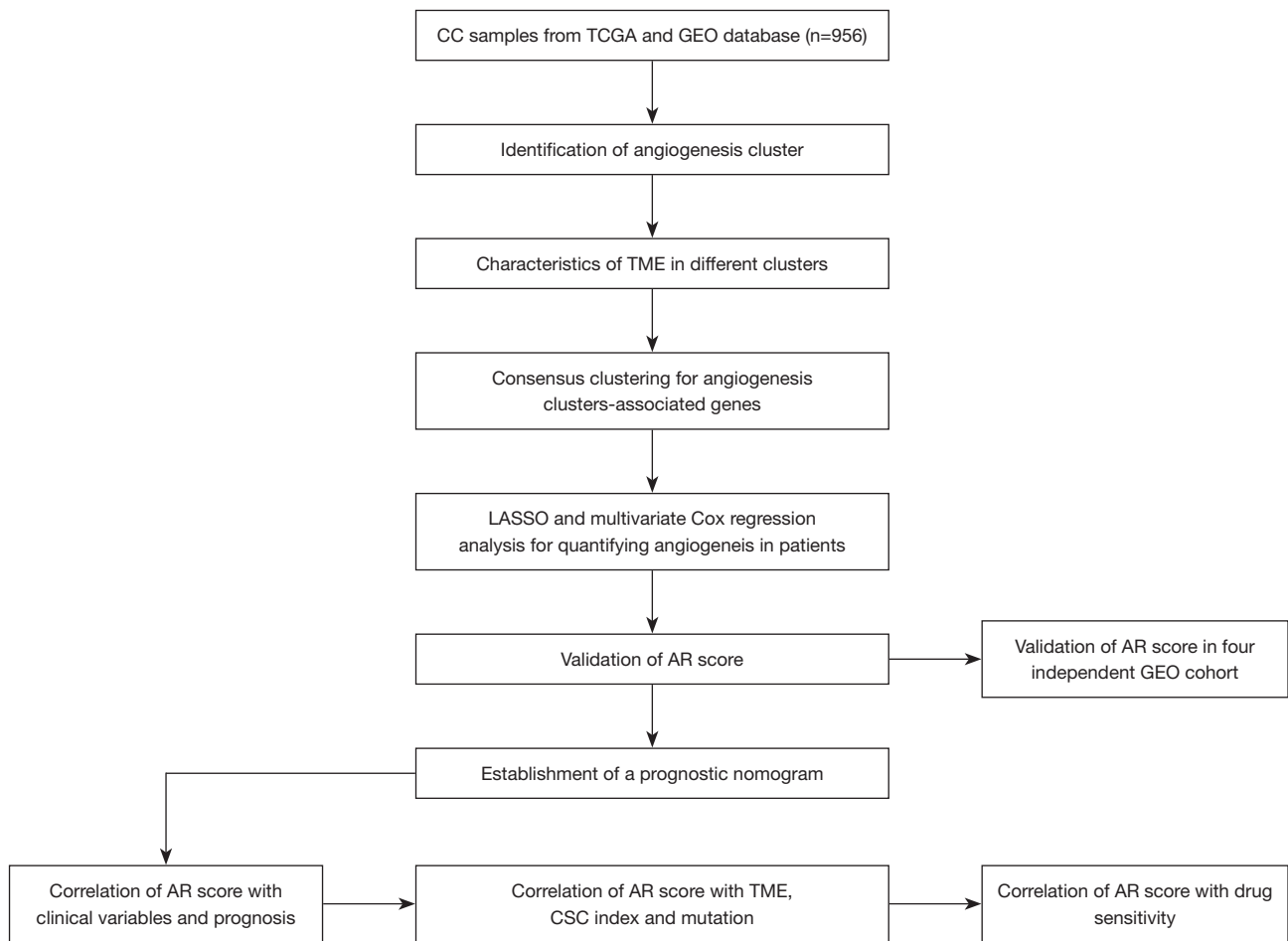


Figure S1 The entire workflow of the study. AR score, angiogenesis-related genes score; CC, colon cancer; CSC, cancer stem cell; GEO, gene expression omnibus; TCGA, the cancer genome atlas program; TME, tumor microenvironment; MSI, microsatellite instability.

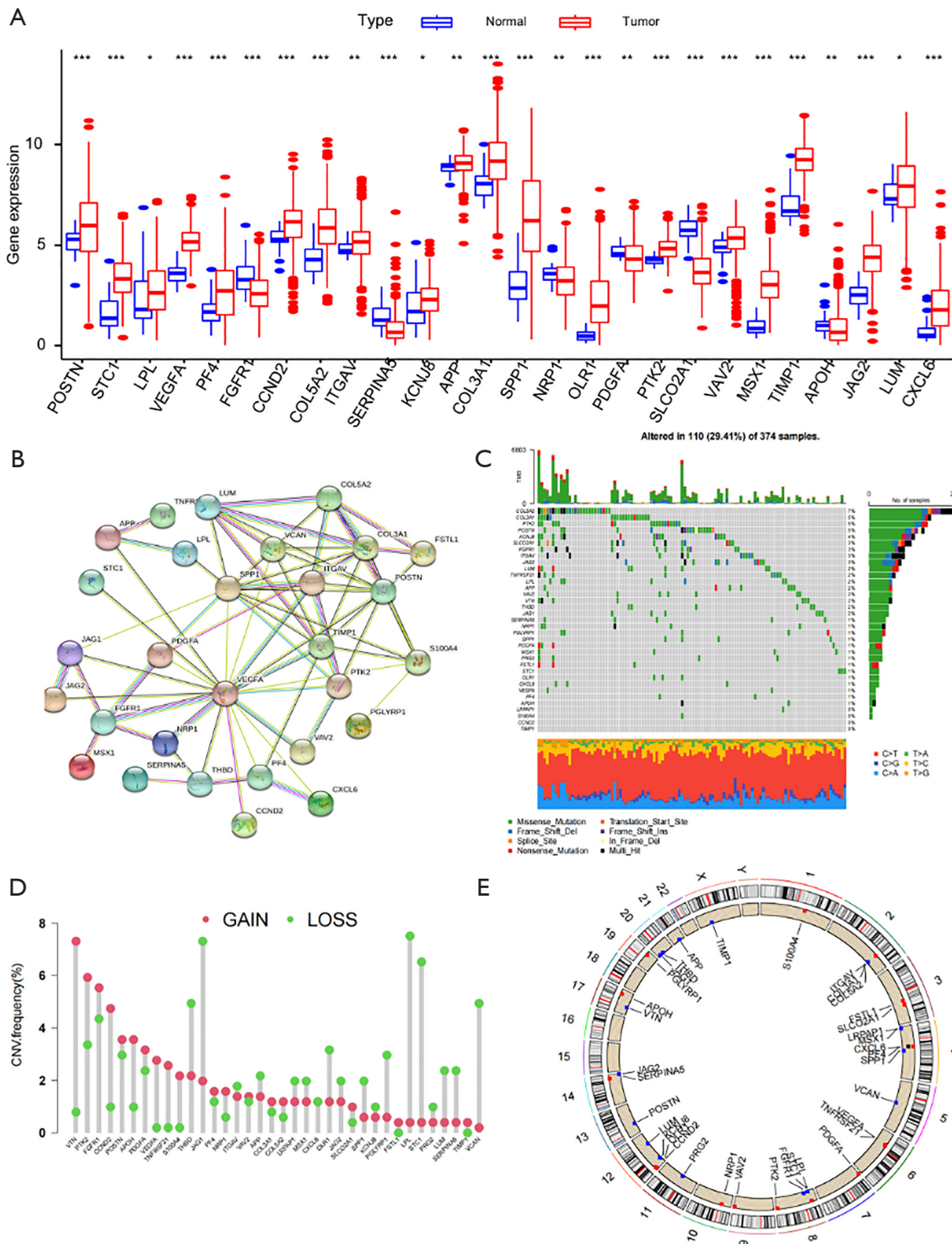


Figure S2 Genetic mutational overview of AAGs in CC. (A) The distribution of gene expression levels for genes that are DEGs in CC compared to normal tissues. (B) A PPI network for these DEGs, retrieved from the STRING database. (C) Genetic changes specific to AAGs. (D) Frequencies of CNV such as gains, losses, and non-CNVs among AAGs. (E) Circus plots depicting the chromosomal distribution of AAGs. Statistical significance is indicated by asterisks. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$. AAG, angiogenesis-associated gene; CC, colon cancer; CNV, copy number variation; DEG, differentially expressed gene; PPI, protein-protein interaction.

Table S2 The prognostic values of angiogenesis-associated genes in colon cancer patients

ID	Hazard ratio (HR)	HR.95L	HR.95H	P value	km
<i>POSTN</i>	1.086873787	0.981222429	1.203900964	0.110344227	0.005713363
<i>FSTL1</i>	1.148470965	1.010889427	1.304777279	0.033476402	0.000771989
<i>LRPAP1</i>	0.935416792	0.699756994	1.250440628	0.65212266	0.043238747
<i>STC1</i>	1.188757237	1.060569952	1.332438059	0.002977026	0.002783602
<i>LPL</i>	1.016499596	0.928853119	1.112416386	0.722053668	0.102340853
<i>VEGFA</i>	1.226106219	1.018342487	1.476258214	0.031410043	0.001636285
<i>PF4</i>	0.963507322	0.875230365	1.060688016	0.448304145	0.051196526
<i>THBD</i>	1.115791074	0.96673585	1.287828231	0.134247189	0.009215346
<i>FGFR1</i>	1.209647021	1.004200734	1.45712492	0.045058939	0.011594061
<i>TNFRSF21</i>	1.108958682	0.899368378	1.367392258	0.333230856	0.015242505
<i>CCND2</i>	0.973736484	0.877783383	1.080178503	0.615086772	0.028614821
<i>COL5A2</i>	1.145509127	1.038276102	1.263817166	0.006748877	0.000443341
<i>ITGAV</i>	1.096748602	0.942352523	1.276441106	0.232885561	0.088525352
<i>SERPINA5</i>	1.088848728	0.902742866	1.313321431	0.373426552	0.009115728
<i>KCNJ8</i>	1.27456596	1.104362923	1.471000476	0.000908775	1.34E-07
<i>APP</i>	1.08197231	0.843672612	1.387580992	0.534793228	0.190468482
<i>JAG1</i>	0.97727564	0.770416504	1.239677072	0.849758329	0.399693357
<i>COL3A1</i>	1.131196248	1.024027737	1.249580363	0.015202533	4.68E-06
<i>SPP1</i>	1.07313916	1.000843959	1.15065655	0.047292533	0.001179079
<i>NRP1</i>	1.15366427	0.958405715	1.388703371	0.130811962	0.004848193
<i>OLR1</i>	1.121804508	1.021484011	1.231977535	0.016186622	0.000178118
<i>PDGFA</i>	0.996713145	0.856225673	1.160251467	0.96612244	0.208654042
<i>PTK2</i>	1.048700379	0.854323466	1.28730221	0.649369352	0.066911718
<i>SLCO2A1</i>	1.029740511	0.904517197	1.172300012	0.657762304	0.094165575
<i>PGLYRP1</i>	1.085398078	0.801887317	1.469145306	0.595736882	0.062167879
<i>VAV2</i>	1.285830298	1.077952041	1.533796951	0.005201901	0.00347325
<i>S100A4</i>	1.077815029	0.967620258	1.200559028	0.173262406	0.023354421
<i>MSX1</i>	1.069996624	0.961052804	1.191290186	0.216878063	0.017529111
<i>TIMP1</i>	1.327256857	1.138781152	1.54692652	0.000291129	5.55E-06
<i>APOH</i>	0.781422053	0.644224728	0.947837608	0.012286359	0.004531509
<i>PRG2</i>	0.845745631	0.485051478	1.474659299	0.554771996	0.062584988
<i>JAG2</i>	1.143112358	0.989719725	1.32027869	0.068850052	0.000573502
<i>LUM</i>	1.074949181	0.972783569	1.187844633	0.156068703	0.013186383
<i>CXCL6</i>	0.998253685	0.91168601	1.093041253	0.969875259	0.049105247

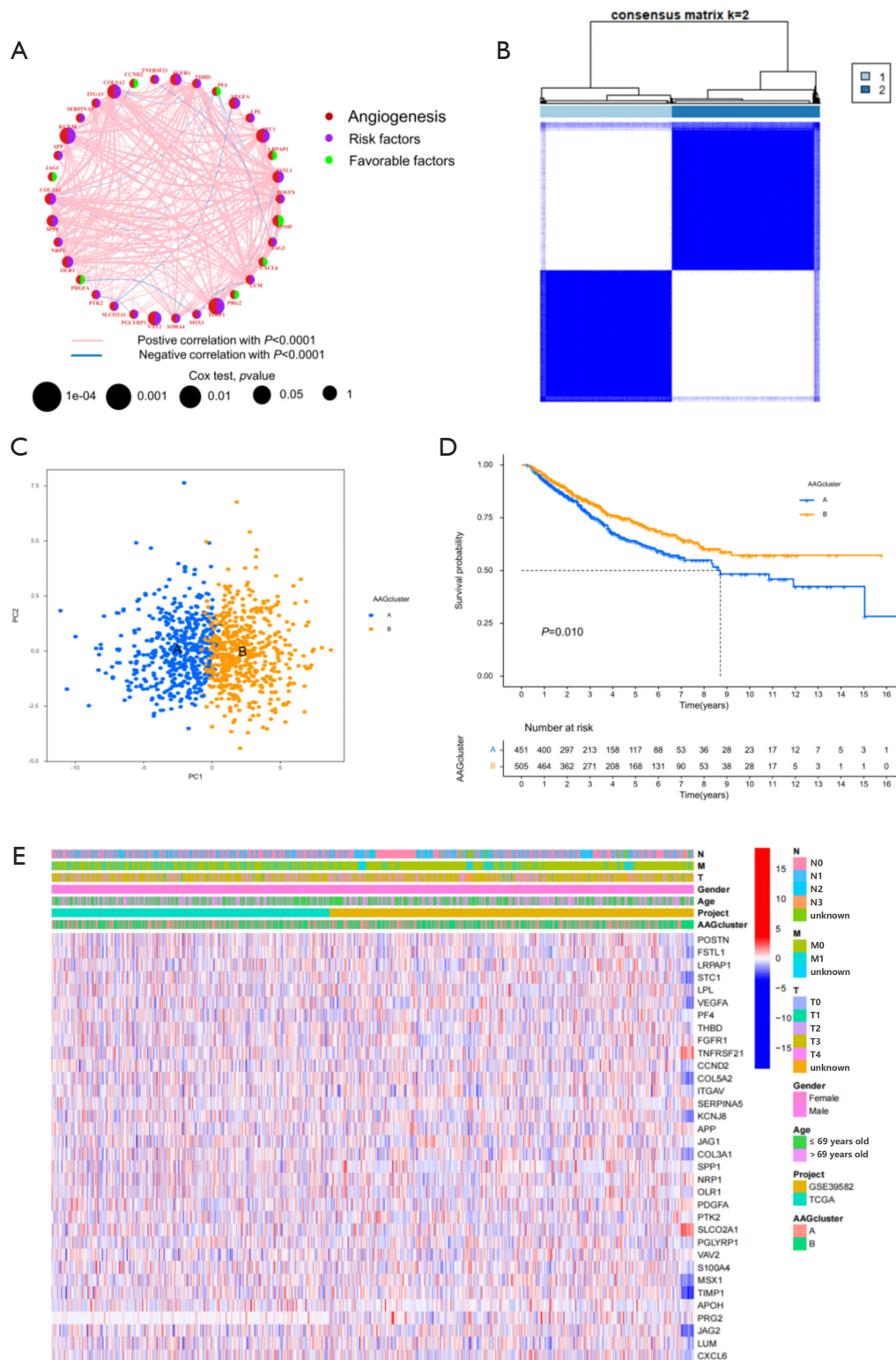


Figure S3 Subgrouping of AAGs and their clinicopathological and biological traits in two distinct sample subtypes defined by consistent clustering. (A) A correlation network encompassing AAGs in the TCGA dataset. (B) A consensus matrix heatmap that outlines two distinct clusters ($k=2$) and their respective areas of correlation. (C) A PCA plot, highlighting significant transcriptome differences between the two AAG subgroups. (D) A univariate analysis that reveals AAGs significantly associated with OS. (E) Comparison of clinicopathological features and expression profiles of AAGs across the two identified subgroups, emphasizing their differences. AAG, angiogenesis-associated gene; OS, overall survival; PCA, principal component analysis; TCGA, The Cancer Genome Atlas.

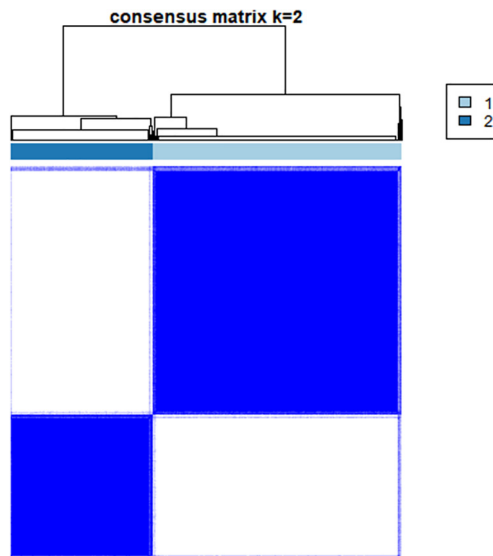


Figure S4 Identification of distinct gene subtypes utilizing DEGs within two angiogenesis subgroups in the CC cohort. CC, colon cancer; DEG, differentially expressed gene.

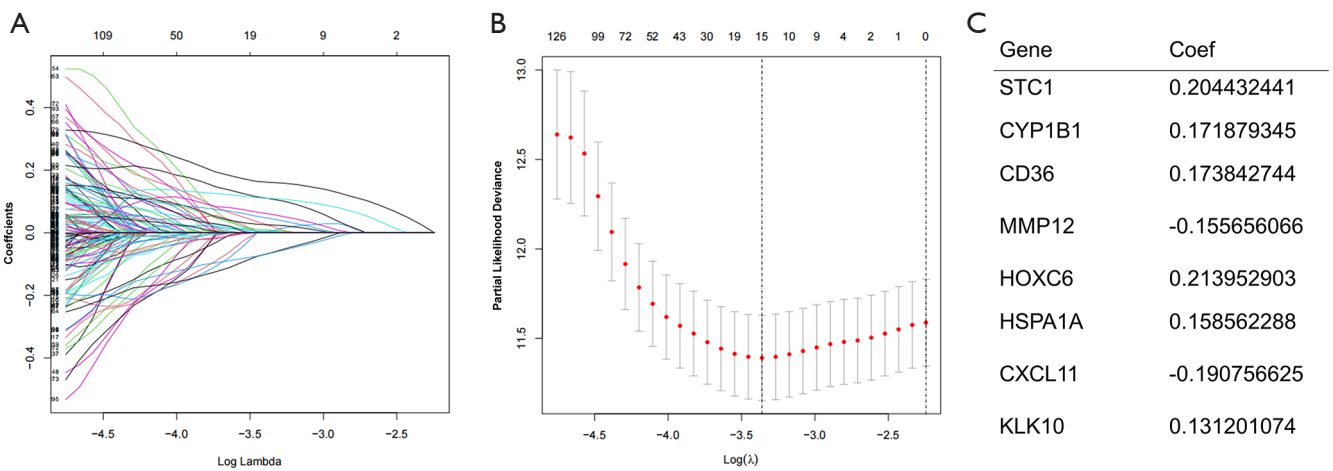


Figure S5 Identifying potential prognostic genes through a representative selection process. (A,B) The application of LASSO regression analysis, along with partial likelihood deviance, to identify prognostic genes. (C) The findings of multivariate Cox regression analysis conducted on these prognostic genes. LASSO, least absolute shrinkage and selection operator.

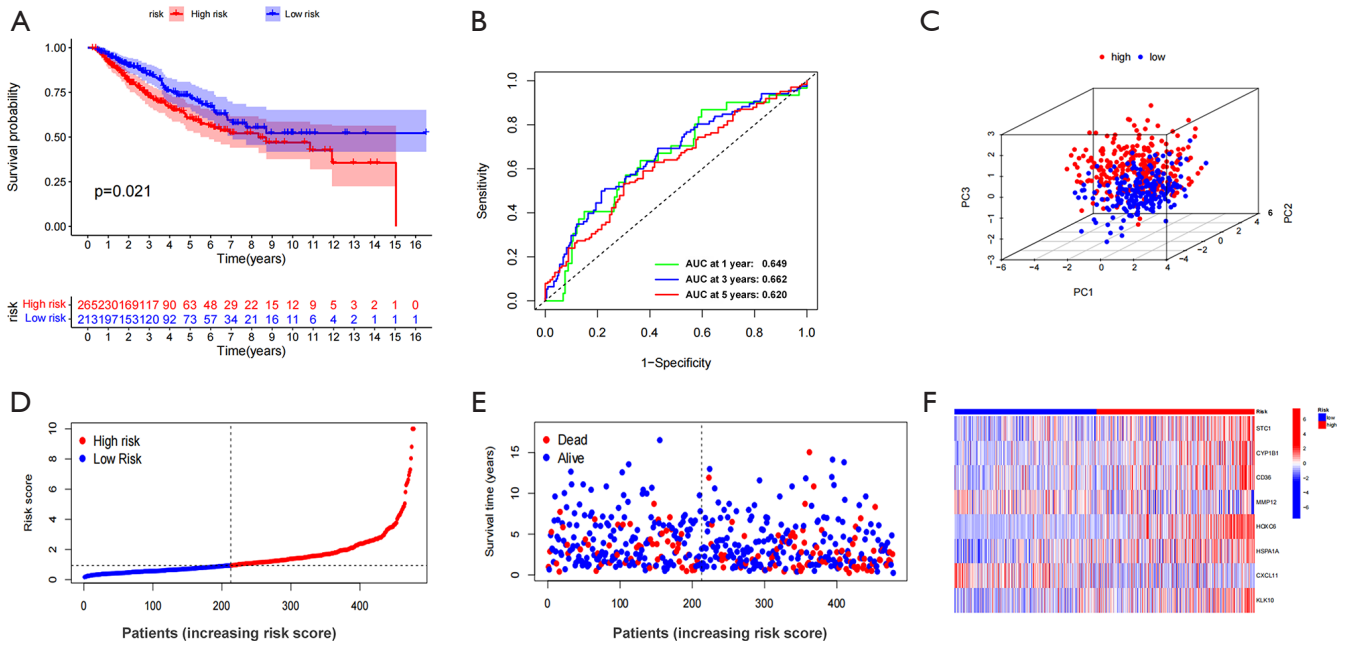


Figure S6 Validation of the AR score in an independent test cohort. (A) Kaplan-Meier survival analysis comparing OS between two patient groups stratified by the AR score. (B) ROC curves assessing the predictive accuracy of 1-, 3-, and 5-year survival based on the AAG score, measuring both sensitivity and specificity. (C) Three-dimensional PCA illustrating distinct spatial distributions of patients from different risk groups. (D,E) Ranked dot plot visualizing the distribution of AR scores across patients, accompanied by a scatter plot depicting individual patient survival status. (F) Expression profiles of eight key prognostic genes in high-risk versus low-risk patient subgroups. AAG, angiogenesis-associated gene; AR score, angiogenesis-related genes score; OS, overall survival; KM, Kaplan-Meier; PCA, principal component analysis.

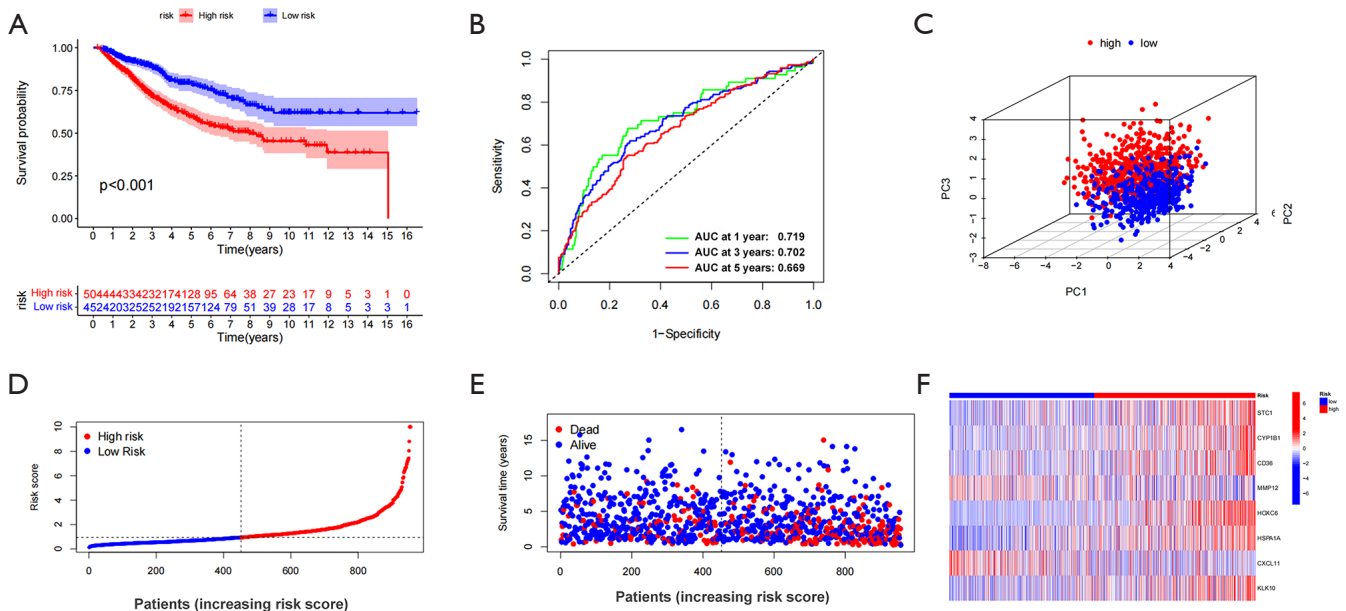


Figure S7 Validation of AR score in the entire cohort. (A) KM analysis of the OS between the two groups. (B) ROC curves to predict the sensitivity and specificity of 1-, 3-, and 5-year survival according to the AAG score. (C) The 3D PCA analysis demonstrated that the patients in the different risk groups were distributed in two directions. (D,E) The ranked dot plot indicates the AR score distribution and scatter plot presenting the patients' survival status. (F) Expression patterns of 8 selected prognostic genes in high- and low-risk groups. AAG, angiogenesis-associated gene; AR score, angiogenesis-related genes score; KM, Kaplan-Meier; OS, overall survival; ROC, receiver operating characteristic; PCA, principal component analysis

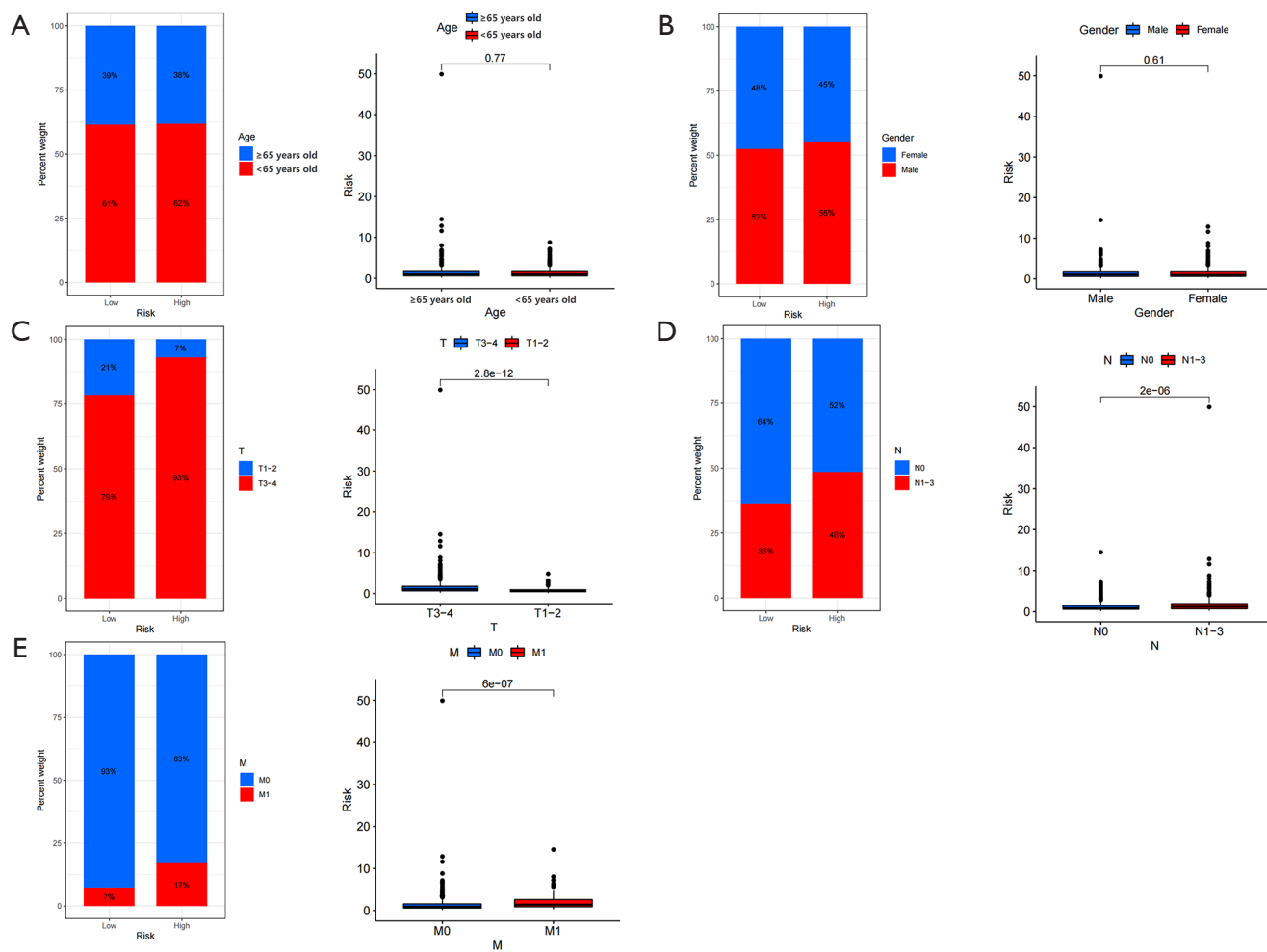


Figure S8 The correlation analysis of AR score and clinicopathological variables in CC. The (A) Age, (C) T-stage and (E) M-stage distribution of with patients in different risk groups. The correlation between the AR score and (B) Gender, and (D) N-stage. AR score, angiogenesis-related genes score; CC, colon cancer.

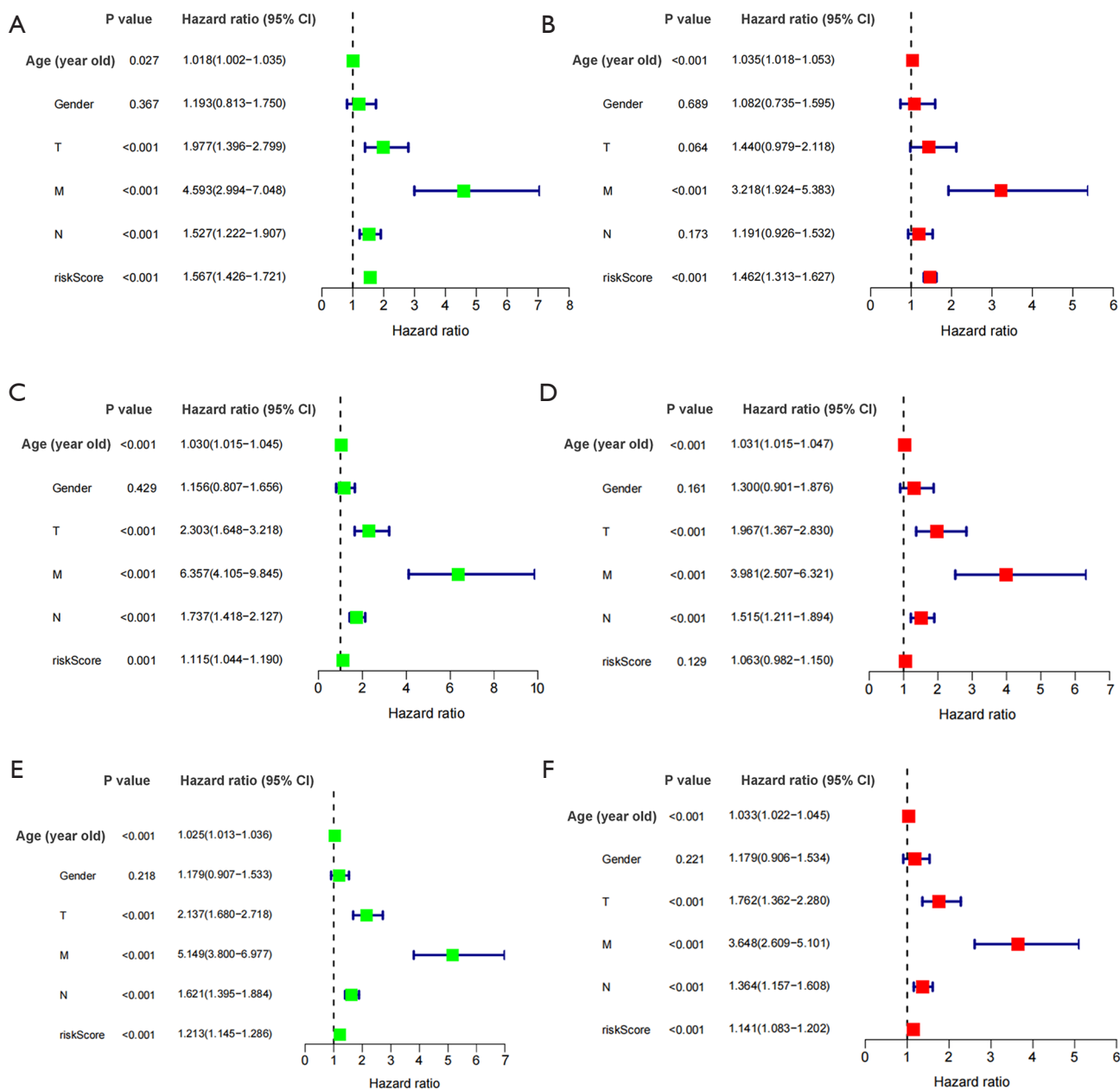


Figure S9 The independent prognosis analysis of AR score and clinicopathological variables in CC. (A,B) Univariate and multivariate analyses showed the prognostic value of the AR score in the training cohort. (C,D) Univariate and multivariate analyses showed the prognostic value of the AR score in the test cohort. (E,F) Univariate and multivariate analyses showed the prognostic value of the AR score in the entire cohort. AR score, angiogenesis-related genes score; CC, colon cancer.

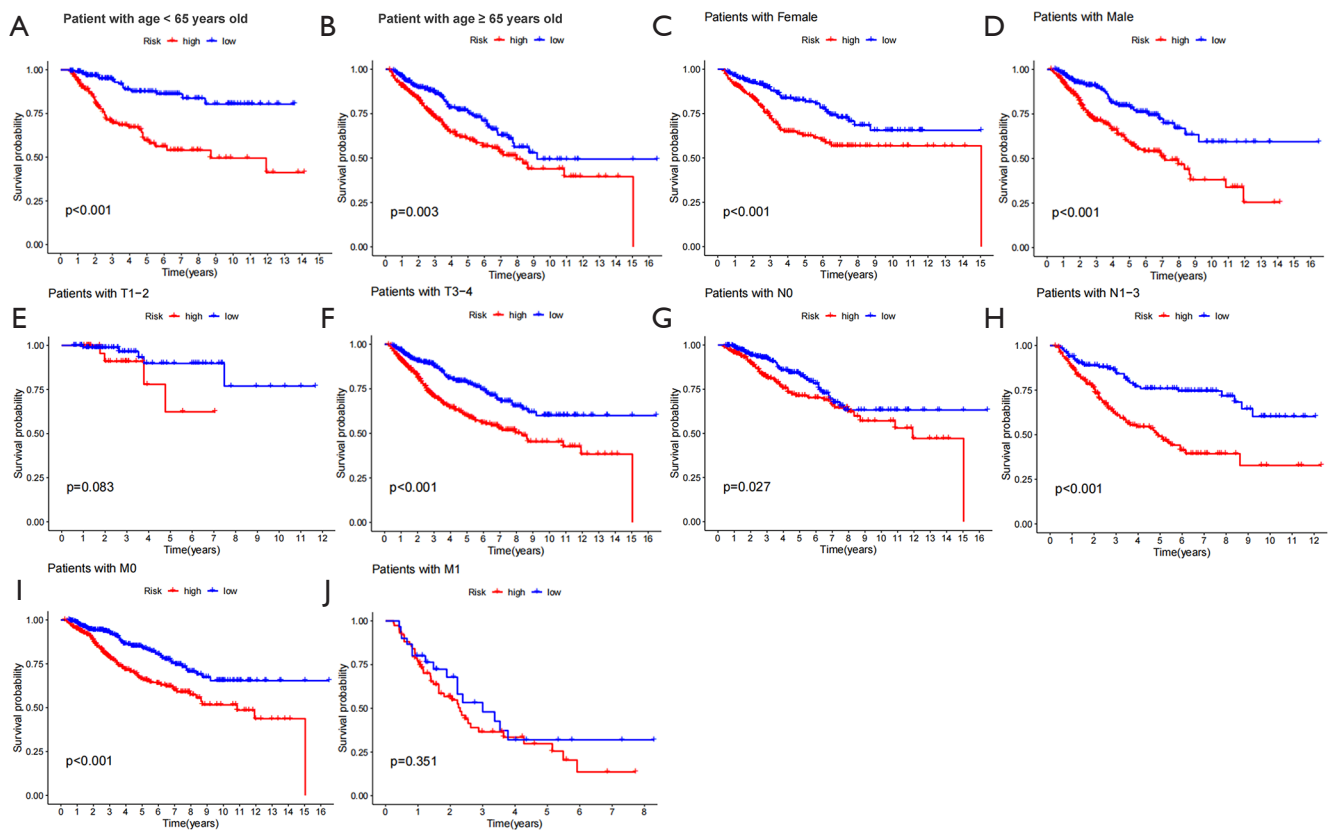


Figure S10 Stratification analysis of the AR score in CC. (A,B) Age (age <65 and age ≥60 years old). (C,D) Gender (male and female). (E,F) T-stage (T1–2 and T3–4). (G,H) N-stage (N0 and N1–3) (I,J) M-stage (M0 and M1). AR score, angiogenesis-related genes score; CC, colon cancer.

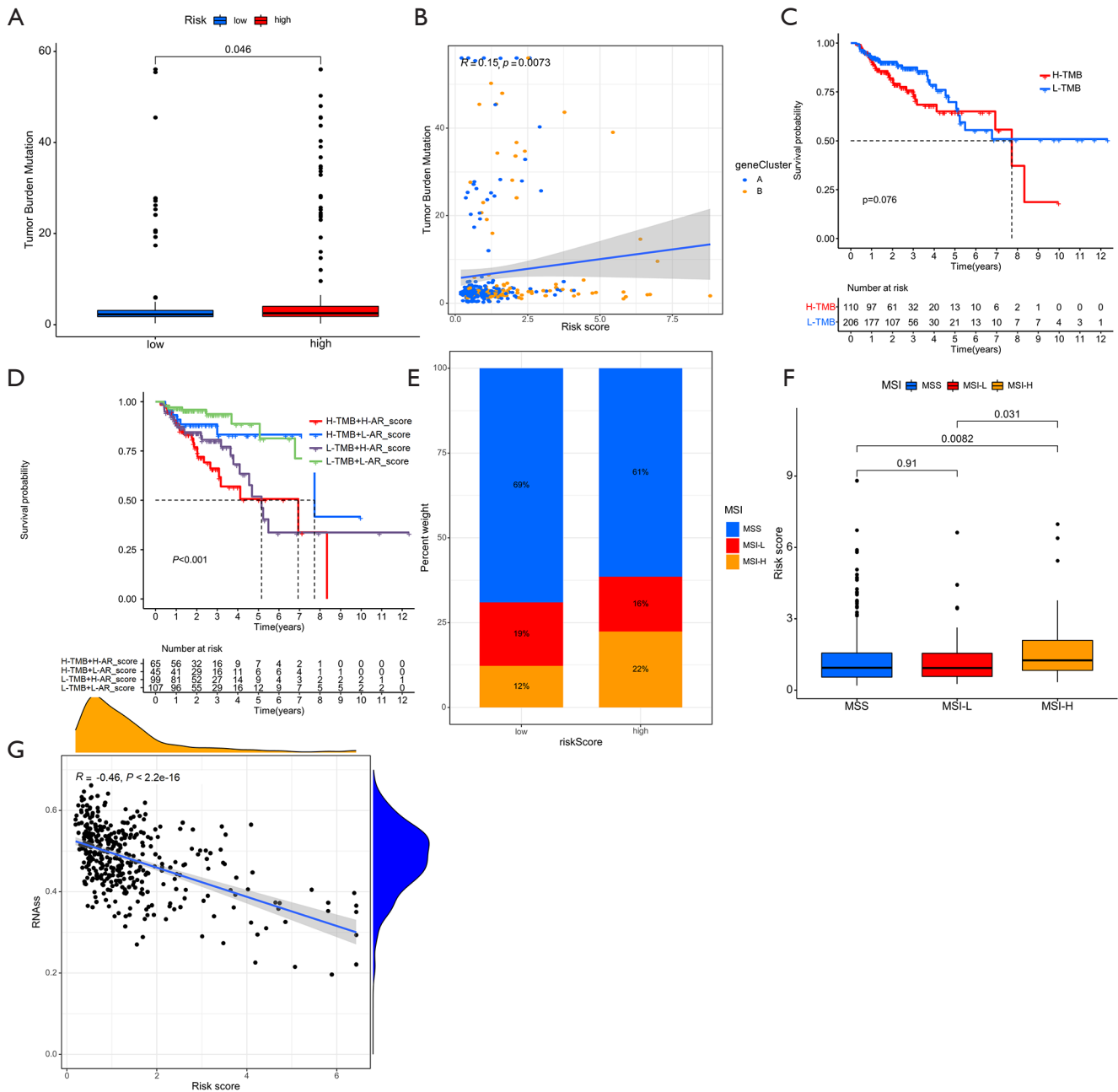


Figure S11 Comprehensive analysis of the AR score in CC. (A,B) Relationships between AR score and TMB. (C) Kaplan-Meier analysis of the OS between the low- and high-TMB groups. (D) Survival analysis among four patient groups stratified by both TMB and AR score. (E,F) Relationships between AR score and MSI. (G) Relationships between AR score and CSC index. AAG, angiogenesis-associated gene; AR score, angiogenesis-related genes score; CC, colon cancer; TMB, tumor mutation burden; MSI, microsatellite instability; CSC, cancer stem cell.

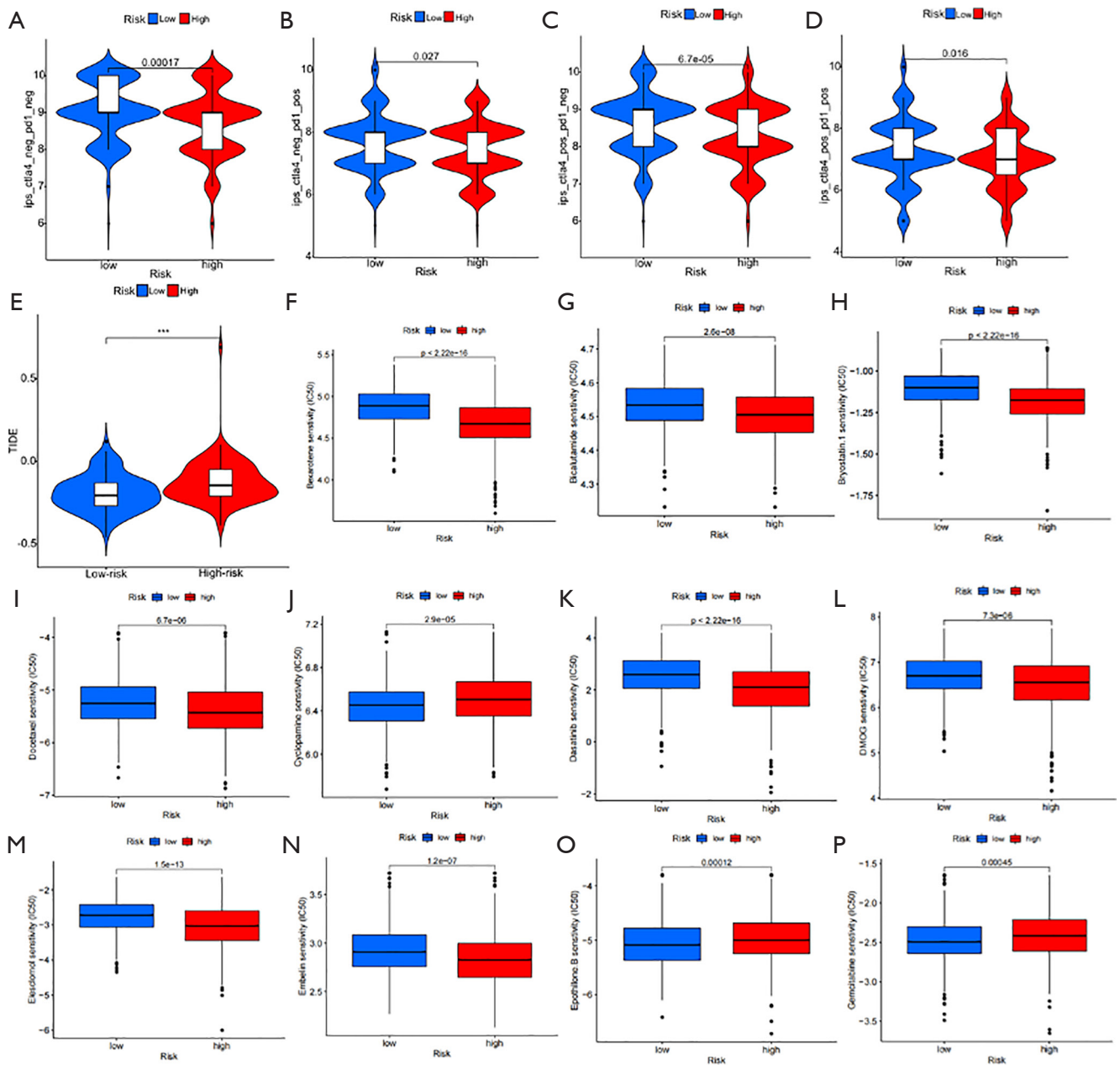


Figure S12 Drug sensitivity analysis of common chemotherapeutic drugs. ***, $P < 0.001$.

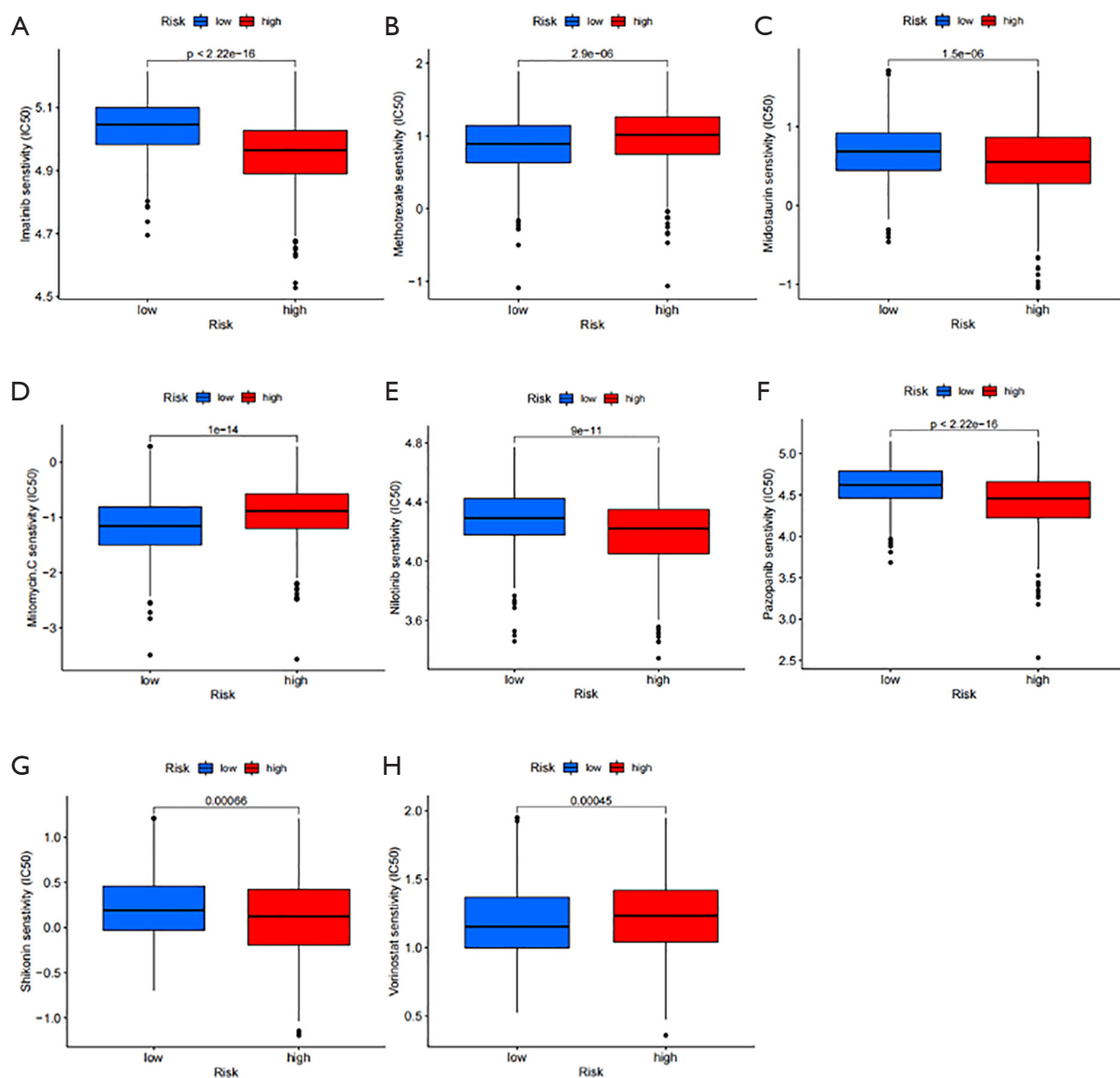


Figure S13 Drug sensitivity analysis of common chemotherapeutic drugs.