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Analysis of the immune regulatory role and prognostic value of MMP14 in head and neck squamous cell carcinoma

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Abstract

Background

Head and neck squamous cell carcinoma (HNSCC) is one of the most common malignant tumors. Despite advancements in surgery, radiotherapy, chemotherapy, immunotherapy, and targeted therapy, the recurrence and mortality rates of HNSCC remain alarmingly high. Matrix metalloproteinase 14 (MMP14) is closely linked to the onset and progression of various malignant tumors; however, the specific mechanisms underlying its role in HNSCC are not fully elucidated.

Methods

This study employed public datasets from TCGA, GTEx, GEPIA2, TIMER, and LinkedOmics to analyze the expression levels, biological functions, immune infiltration patterns, clinical relevance, and prognostic significance of MMP14 in HNSCC. Analyses included differential gene expression, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses, Kaplan-Meier survival analysis, ROC analysis, and Cox regression modeling. Additionally, immunohistochemical (IHC) verification was conducted using paired tumor and adjacent normal tissues from HNSCC patients.

Results

The results revealed that MMP14 is significantly overexpressed in HNSCC, with primary functions associated with extracellular matrix (ECM)-receptor interactions and cell adhesion. MMP14 expression positively correlates with the infiltration of macrophages and eosinophils, while lower levels of MMP14 are linked to increased infiltration of CD8 + T cells and cytotoxic immune cells. ICH analysis corroborated the elevated expression of MMP14 in tumor tissues. Clinical assessments indicated that high MMP14 expression significantly correlates with advanced pathological stages, lymphovascular invasion, lymph node metastasis, adverse treatment responses, and poorer survival outcomes. Furthermore, MMP14 exhibited high diagnostic accuracy and effectively predicted the survival rates of HNSCC patients in prognostic models.

Conclusions

MMP14 is highly expressed in HNSCC and is associated with the initiation, progression, and poor prognosis of this malignancy. These findings suggest that MMP14 may serve as a potential biomarker for the diagnosis, treatment, and prognostic evaluation of HNSCC.

Introduction

Head and neck squamous cell carcinoma (HNSCC) is a malignant tumor of epithelial origin that can occur in the nasal cavity, oral cavity, pharynx, and larynx[1–3]. It exhibits a relatively high incidence and mortality rate globally. According to the 2022 global cancer statistics, approximately 892,000 news cases of HNSCC were reported, with about 458,000 deaths attributed to the disease. This malignancy accounted for 4.4% of all new cancer cases worldwide and 4.7% of cancer-related deaths[4]. The etiology of HNSCC is multifactorial, stemming from a combination of lifestyle and environment influences. Key risk factors include smoking, alcohol consumption, betel nut chewing, and infections with HPV and EBV[5–7]. Genetic predispositions, radiation exposure, and immune status also contribute to the risk. Despite significant advancements in treatment, HNSCC remains challenging to detect in its early stages due to the absence of specific clinical manifestations. By the time symptoms become apparent, many patients have already progressed to stage III or IV[8, 9]. While comprehensive treatment modalities-including surgery, radiotherapy, chemotherapy, immunotherapy, and targeted therapy- have been developed, the prognosis and quality of life for patients with HNSCC continue to be suboptimal[10]. This is particularly true for individuals in the middle and advanced stages, where recurrence and metastasis are the leading causes of treatment failure and mortality. Statistically, the 5-year survival rate for HNSCC is less than 65%. Therefore, investigating the molecular mechanisms underlying HNSCC progression and identifying stable, reliable prognostic biomarkers and potential therapeutic targets is critical for achieving precision treatment and improving patient outcomes.

MMP14, or membrane-type 1 matrix metalloproteinase (MT1-MMP), is a significant member of the MMP family[11]. Numerous studies have shown that MMP14 is highly expressed in various malignancies, including ovarian cancer, melanoma, colorectal cancer, uterine leiomyosarcoma, and HNSCC, often correlating with increased migration, invasion and poor prognosis[12–16]. As a protease located on the cell membrane, MMP14 plays a critical role in the degradation and remodeling of the ECM. It directly hydrolyzes various core ECM components, such as structurally dense type I, II, and III collagens and fibronectin, effectively dismantling physical barriers and facilitating the local infiltration and distant dissemination of tumor cells[17]. Furthermore, MMP14 promotes tumor cell proliferation and migration by cleaving cell adhesion molecules, regulating intercellular junctions, and modulating apoptosis-related molecules and signaling pathways [18–20].

While extensive research highlights the significant role of MMP14 in the progression of various tumors, its specific molecular mechanism, clinical relevance, and impact on patient prognosis in HNSCC have not yet been systematically elucidated. This study aimed to explore the role of MMP14 in the occurrence and progression of HNSCC and evaluate its potential as a biomarker or therapeutic targe. The investigation assessed the expression, immune infiltration, functional enrichment of MMP14 in HNSCC, and its associations with clinical pathological features and prognosis based on comprehensive public databases and bioinformatics analysis. The finding seek to provide new insights and theoretical foundation for understanding the role of MMP14 in HNSCC.

Materials and methods

Data acquisition and expression analysis

RNA sequencing data and corresponding clinical information of patients with HNSCC were obtained from The Cancer Genome Atlas (TCGA) database. Expression data form normal tissue were supplemented using the Genotype-Tissue Expression (GTEx) project. The expression profile of MMP14 across multiple tumor types was analyzed using GEPIA2, an online platform integrating TCGA and GTEx datasets. Differential expression analysis between tumor and adjacent normal tissues was conducted, with the expression distribution of MMP14 in HNSCC was visualized using boxplots and volcano plots.

Differentially expressed gene analysis

Differentially expressed genes (DEGs) between HNSCC tissues and normal tissues were identified based on TCGA transcriptome data. Genes exhibiting an adjusted $P < 0.05$ and |log2 fold change (FC)| > 1 were considered significantly differentially expressed. Volcano plots were generated to visualize upregulated and downregulated genes.

Functional enrichment analysis

To elucidate the potential biological functions and molecular mechanisms of MMP14 in HNSCC, Gene Ontology (GO) enrichment analysis -which encompasses biological process (BP), cellular component (CC), and molecular function (MF) -alongside Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, was performed on DEGs associated with MMP14. The KEGG pathway enrichment analysis is based on the KEGG database (https://www.genome.jp/kegg/) and related annotation information. Bubble charts were employed to illustrate the enriched signaling pathways and biological functions[21].

Co-expression analysis of MMP14

The co-expression network of MMP14 in HNSCC was analyzed through the LinkedOmics database. Pearson correlation analysis was conducted to identify genes that are positively and negatively correlated with MMP14 expression. Volcano plots and heatmaps were generated to present the top correlated genes. Furthermore, KEGG enrichment analysis of co-expressed genes was performed to investigate the biological pathways linked to MMP14.

Immune infiltration analysis

The relationship between MMP14 expression and immune cell infiltration in HNSCC was evaluated using the TIMER database. Correlation analyses evaluated the relationship between MMP14 expression and various immune cell subsets, including macrophages, NK cells, $CD4^+$ T cells, $CD8^+$ T cells, dendritic cells,

and regulatory T cells. Scatter plots and heatmaps visualized these correlations. Additionally, immune infiltration scores between high- and low-MMP14 expression groups were compared to assess the influence of MMP14 on the tumor immune microenvironment. All procedures involving human specimens were conducted in accordance with the Declaration of Helsinki and relevant institutional and national guidelines and regulations. The study protocol was reviewed and approved by the Institutional Review Board/Ethics Committee of The First Affiliated Hospital of Kunming Medical University (Approval No. (2023) Ligation Review No. 98). All experimental protocols involving human tissues were performed in accordance with the approved guidelines. Written informed consent was obtained from all participants or their legal guardians prior to sample collection and participation in this study.

Immunohistochemical staining

Tumor tissues and paired adjacent normal tissues were collected from three patients with HNSCC for immunohistochemical (IHC) analysis. Tissue sections were fixed, paraffin-embedded, and treated with anti-MMP14 primary antibody according to standard protocols. The staining intensity and localization of MMP14 were observed under a light microscope to evaluate protein expression differences between tumor and adjacent tissues.

Clinical correlation analysis

Associations between MMP14 expression and clinicopathological characteristics-including pathological stage, clinical stage, lymphovascular invasion, radiotherapy status, lymph node neck dissection, and treatment response-were analyzed using clinical data from TCGA. Differences in MMP14 expression across various clinical subgroups were assessed and visualized using boxplots.

Survival and prognostic analysis

Kaplan–Meier survival analysis was conducted to evaluate the association between MMP14 expression and overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) in HNSCC patients. Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic value of MMP14. Univariate and multivariate Cox regression analyses were executed to identify independent prognostic factors influencing HNSCC survival. A prognostic nomogram, integrating MMP14 expression with clinicopathological factors, was subsequently developed to predict 1-, 3-, and 5-year survival probabilities.

Statistical analysis

All statistical analyses and graphical visualizations were conducted utilizing R software (version 4.3.1) and GraphPad Prism (version 9.0). Continuous variables between two groups were compared using

Student's *t*-test, while comparisons among multiple groups were conducted via one-way analysis of variance (ANOVA). Survival curves were generated using the Kaplan–Meier method and compared through the log-rank test. Pearson correlation analysis was applied to evaluate the correlations between MMP14 expression and immune infiltration levels. A two-sided *P* value < 0.05 was considered statistically significant.

Results

MMP14 expression in HNSCC

Lineage analysis of the MMP family in HNSCC was conducted using GEPIA2, revealing the MMP14 expression was relatively upregulated (Fig. 1A). Examination of mRNA levels of MMP14 in tumor tissues and adjacent normal tissues across 33 cancer types, utilizing TCGA and GTEx data, indicated that MMP14 was highly expressed in numerous cancers, including BLCA, BRCA, CHOL, COAD, ESCA, HNSCC, KIRC, KIRP, LIHC, LUAD, LUSC, READ, STAD, THCA (Fig. 1B). Compared to normal tissues, MMP14 expression was significantly elevated in HNSCC (Fig. 1C). A volcano plot illustrated the differences in gene expression among HNSCC samples, identifying a total of 18,756 DEGs, which included 498 upregulated genes and 1,483 downregulated genes (Fig. 1D).

Mechanism Study of MMP14 in HNSCC

To elucidate the mechanism of MMP14 in HNSC, enrichment analysis of the DEGs was performed, with results presented in bubble charts indicating the enrichment status across biological processes, cellular components, and molecular functions (Fig. 2A). Analysis via LinkedOmics was utilized to further examine the expression and biological functions of MMP14 in HNSCC. As illustrated in the volcano plot (Fig. 2B), the red curve and the points within the high significance region on the right indicate genes such as COL5A1 and FN1, which exhibit a strong positive correlation with MMP14 along with significant results. Conversely, the green curve and points in the left region represent genes such as SLC25A30 and RAPGEF1, indicating significant negative correlations. Heatmaps were employed to display the top 50 genes in HNSCC that positive and negative correlate with MMP14 expression (Fig. 2C-D). KEGG analysis revealed that co-expressed genes were associated with ECM-receptor interaction, focal adhesion, protein digestion and absorption, hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), amoebiasis, and more. These findings suggest that the upregulated pathways were concentrated in ECM, cell adhesion, and heart-related functions, whereas downregulated pathways were associated with fundamental biological processes such as translation, energy metabolism, and DNA repair (Fig. 2E).

Analysis of MMP14 Expression and Immune Infiltration

To clarify the correlation between MMP14 expression characteristics in HNSCC and the infiltration of the tumor immune microenvironment, the TIMER database was utilized to evaluate the association between MMP14 expression levels and the abundance of various immune cell infiltrations. Correlation heatmap analysis indication that MMP14 expression was significantly positively correlated with the infiltration of multiple immune cells ($p < 0.05$), with the strongest correlations noted for macrophages, eosinophils,

and NK cells. Additionally, there were significant positive correlations with effector T cells (Tcm, Tem) and regulatory T cells (TReg), suggesting that MMP14 may play a pivotal role in regulating the tumor immune microenvironment (Fig. 3A). A scatter plot analysis was conducted to quantify the relationship between MMP14 expression and key immune cell infiltration while controlling for tumor purity. As shown in Fig. 3B, MMP14 expression exhibited the strongest correlation with $CD4^+$ T cells, followed closely by macrophages. Comparison of the infiltration levels of various immune cell subsets between the low-expression and high-expression MMP14 groups revealed that the low-expression group had significantly higher scores for aDC, B cells, $CD8^+$ T cells, cytotoxic cells, and other immune populations. This finding suggests that lower MMP14 expression is closely associated with increased infiltration of multiple immune cells, implying that MMP14 may inhibit immune infiltration in the tumor microenvironment (Fig. 3C). To further illustrate MMP14 expression, tumor tissues and paired adjacent normal tissues were collected from three HNSCC patients for IHC analysis (Figs. 3D-F). The results demonstrated weak staining for MMP14 in adjacent tissues, indicating low expression, while tumor tissues exhibited strong brownish-yellow positive staining signal. This suggests that MMP14 may play a significant role in the initiation and progression of HNSCC, and holds potential as a biomarker for assessing malignant progression and prognosis in HNSCC.

MMP14 expression and clinical analysis

In HNSCC, the expression level of MMP14 exhibits significant differential expression across various pathological stages. In the pathological T stage, the expression of MMP14 in the T1&T2 and T3&T4 groups is significantly higher than in the normal group, with the expression level in the T3&T4 group exceeding that in the T1&T2 stage. This suggests that MMP14 may facilitate local tumor invasion and promote malignant progression. In the pathological N stage, these findings imply a potential association of MMP14 with the enhanced ability of tumor lymph node metastasis. Notably, in the pathological M stage, MMP14 expression in the M0 group is significantly higher than in both the normal and M1 group, while expression in the M1 group approaches normal levels. This phenomenon may reflect alterations in tumor biological behavior or the remodeling of the microenvironmental matrix(Fig. 4A-C).Clinical analysis further supports these observations. In the clinical T stage, high MMP14 expression was noted in both TI&T2 and T3&T4 groups, indicating a close relationship between MMP14 levels and HNSCC progression. In the clinical N stage, MMP14 expression in the N0, N1, N2 and N3 groups was significantly elevated compared to the normal group, reinforcing its association with tumor metastatic capabilities in HNSCC. Additionally, when comparing normal tissues, the expression of MMP14 in tumor tissues from M0 group patients was significantly increased, suggesting a potential promotive role in tumor development（Fig. 4D-F）.Analysis of radiotherapy status revealed that MMP14 expression in both the non-radiotherapy and radiotherapy groups was significantly higher than in the normal group, indicating that MMP14 may participate in HNSCC progression as well as in radiotherapy-related biological processes. This positions MMP14 as a potential molecular marker for evaluating treatment response and prognosis（Fig. 4G）. MMP14 is also associated with the status of lymphovascular invasion in HNSCC patients. Expression levels of MMP14 in the lymphovascular invasion group were significantly higher than in the normal group, and expression in this group surpassed that of individuals without

lymphovascular invasion. This suggests MMP14's involvement in the invasion of tumor cells into lymphatic vessels and vascular structures, thereby promoting tumor progression（Fig. 4H）.Additionally, analysis of neck lymph node dissection status indicated that MMP14 may be closely related to lymph node metastasis and high invasiveness in HNSCC（Fig. 4I）.In tumor groups with initial treatment responses categorized as PD, SD, PR, and CR, MMP14 expression levels were significantly elevated compared to the normal group. This finding indicates that high MMP14 expression correlates with the malignancy of HNSCC and poor treatment outcomes, suggesting that MMP14 may serve as a potential target for evaluating treatment efficacy and prognosis（Fig. 4J）.

MMP14 expression and prognostic analysis

The Kaplan–Meier survival analysis results indicated that elevated expression of MMP14 correlates with shorter overall survival (OS) (hazard ratio (HR) = 1.39 (1.06–1.83), P = 0.016), disease-specific survival (DSS) (HR = 1.49 (1.05–2.12), P = 0.027), and progression-free interval (PFI) (HR = 1.25 (0.94–1.67), P = 0.120), suggesting that high MMP14 levels promote the progression of HNSCC and are closely associated with poor clinical prognosis for HNSCC patients. This observation supports the potential utility of MMP14 as a prognostic biomarker(Fig. 5A-C). Furthermore, the Receiver Operating Characteristic curve (ROC curve) analysis revealed an area under the curve (AUC) of 0.926, indicating that MMP14 serve as a promising diagnostic and therapeutic biomarker（Fig. 5D）. Cox regression analysis of both pathological and clinical factors demonstrated that in the univariate analysis, pathologic stage, lymphovascular invasion, and radiation therapy were associated with the prognosis of HNSCC patients. In the multivariate analysis, pathological stage III and Stage IV emerged as independent risk factors for poor prognosis in HNSCC patients, whereas radiation therapy was identified as an independent protective factor, suggesting that radiation therapy can enhance the survival rates of HNSCC patients（Table 1）. The construction of a prognostic model based on factors related to HNSCC prognosis indicated that patients with high MMP14 expression, Pathologic stage III and IV, absence of radiotherapy, and lymphovascular invasion experienced significantly poorer prognoses. Additionally, by evaluating patient's Pathological stage, radiotherapy status, and presence or absence of lymphovascular invasion, a total score was calculated. This score can be correlated with 1-year, 3-year, and 5-year survival rates, enabling predictions of patient survival period. This approach provides a vital tool for clinical prognosis assessment and offers insights for individualized diagnostic and treatment strategies（Fig. 5E）.

Table 1
Baseline clinical data of the HNSCC patients with high and low expression of MMP14

Characteristics	Total(N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Pathologic stage	435				
Stage I&Stage II	94	Reference		Reference	
Stage III&Stage IV	341	1.839 (1.236–2.737)	**0.003**	4.134 (2.022–8.453)	**< 0.001**
Clinical stage	489				
Stage I&Stage II	114	Reference			
Stage III&Stage IV	375	1.226 (0.885–1.700)	0.221		
Gender	503				
Female	134	Reference		Reference	
Male	369	0.760 (0.571–1.012)	0.061	0.683 (0.441–1.059)	0.089
Race	487				
Asian	10	Reference			
Black or African American	47	1.178 (0.405–3.425)	0.763		
White	430	0.777 (0.288–2.095)	0.617		
Age	503				
<= 60	247	Reference		Reference	
> 60	256	1.262 (0.964–1.653)	0.090	1.073 (0.712–1.617)	0.737
Radiation therapy	441				
No	154	Reference		Reference	

Characteristics	Total(N)	Univariate analysis		Multivariate analysis		
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value	
Yes	287	0.617 (0.455–0.837)	**0.002**	0.398 (0.254–0.623)	**< 0.001**	
Alcohol history	492					
No	159	Reference				
Yes	333	0.954 (0.718–1.268)	0.745			
Lymphovascular invasion	341					
No	219	Reference		Reference		
Yes	122	1.708 (1.217–2.397)	**0.002**	1.902 (1.238–2.924)	**0.003**	
Lymphnode neck dissection	500					
No	90	Reference		Reference		
Yes	410	0.728 (0.524–1.011)	0.058	0.459 (0.209–1.009)	0.053	

Discussion

HNSCC is the sixth most common malignant tumor worldwide[22]. Despite recent advances advancements in comprehensive treatment strategies, including surgery, radiotherapy, chemotherapy, and targeted therapy, HNSCC patients continue to experience high rates of recurrence and metastasis, poor prognosis, and a median OS of approximately one year[23]. This scenario highlights the urgent need for in-depth research on HNSCC to improve diagnosis, therapeutic, and prognosis frameworks for clinical practice. In this study, bioinformatics analyses were conducted to assess the expression, function, immune involvement, and clinical significance of MMP14 in HNSCC. A prognostic model was constructed to ascertain the survival duration of HNSCC patients, and these findings were further validated through IHC analysis.

MMP14, also referred to as membrane-type 1 metalloproteinase (MT1-MMP), has been shown in various studies to facilitate the occurrence and progression of numerous tumors by degrading the extracellular

matrix (ECM), promoting the formation of invasive pits, and interacting with tissue metalloproteinase inhibitors (TIMPs). It plays a critical role in the diagnosis, treatment, and prognosis of cancer patients in clinical settings[11, 24]. Analysis of TCGA and GTEx data revealed that MMP14 is highly expressed across 33 cancer types. Moreover, compared to normal tissues, MMP14 expression levels in cancer tissues were significantly elevated. This finding further implicates MMP14 in HNSCC progression and suggests its potential as a biomarker for diagnosis and prognosis in HNSCC.

To elucidate the mechanistic role of MMP14 in HNSCC, pathway enrichment analysis was performed. The results indicated that co-expressed genes linked to MMP14 were significantly enriched in pathways such as ECM-receptor interaction and focal adhesion, suggesting that MMP14 may promote HNSCC invasion and metastasis by regulating ECM remodeling and cell adhesion signaling pathways. Previous studies have reported that MMP14 can modulate melanoma progression through extracellular matrix remodeling and also drive invasion and dissemination in Ewing sarcoma[25, 26]. In summary, MMP14 is crucial in the initiation and progression of HNSCC. Its elevated expression significantly enhances the invasive and metastatic potential of tumor cells, indicating that MMP14 holds promise as a diagnostic marker and therapeutic target for HNSCC.

Furthermore, numerous studies have demonstrated that MMP14 is associated with immune cell infiltration in various malignant tumors, including colon cancer. Similarly, an in-depth analysis of MMP14 and immune cell infiltration in HNSCC revealed a correlation between MMP14 expression levels and the infiltration of various immune cells, such as macrophages and eosinophils. Notably, In the low MMP14 expression group, the infiltration levels of several anti-tumor immune cells, including $CD8^+$ T cells and cytotoxic cells, were significantly higher. This suggests that elevated MMP14 expression contributes to the establishment of an immunosuppressive microenvironment, providing a further avenue for in-depth investigation of HNSCC. Additionally, IHC results corroborated that high MMP14 expression promotes the onset and progression of HNSCC.

Based on the clinical relevance analysis, the high expression of MMP14 is closely associated with advanced tumor stage, lymphatic vessel invasion, and lymph node invasion. Additionally, studies indicate that MMP14 can regulate the functions of extracellular and cell membrane-related proteins, altering cellular interactions and the relationship between cells and the ECM. This regulation can lead to matrix degradation, structural remodeling, and other processes that facilitate the progression of malignant tumors[27]. In the clinical-related analysis presented herein, the expression of MMP14 in the M1 group returned to levels nearly approaching normal, supporting the notion that MMP14 may regulate the remodeling of the microenvironment matrix and highlighting its significant role in the malignant progression of HNSCC. However, the precise mechanism underlying these observations remain to be further elucidated.

Survival analysis revealed a strong correlation between high MMP14 expression and decreased survival rates for HNSCC patients. Moreover, Cox regression analysis identified lymphovascular invasion and pathological stage as independent risk factors, while radiotherapy emerged as an independent protective

factor. These findings can guide clinical assessments of risk, prognosis, efficacy, and individualized treatment plans for tumors. The prognostic model constructed from these related factors effectively predicts survival rates of HNSCC patients, highlighting the importance of MMP14 in the initiation and development of HNSCC, thereby suggesting its potential as a clinical biomarker.

Conclusion

In summary, the analysis of MMP14 expression, biological functions, immune infiltration, clinical characteristics, and prognosis in HNSCC demonstrates that MMP14 is highly expressed in this type of cancer and is linked to ECM remodeling and immune infiltration. Furthermore, MMP14 expression is closely related to tumor stage, lymphovascular invasion, lymph node metastasis, and unfavorable treatment outcomes. These findings suggest that MMP14 may serve as a potential biomarker for the diagnosis, treatment, and prognosis of HNSCC. Nevertheless, the current analyses represent only an initial exploration; further in-depth investigations into its precise mechanisms are necessary to fully understand the implications of MMP14 in HNSCC.

Declarations

Consent for publication:

All authors have read and agreed to the published version of the manuscript.

Competing interests:

The authors declare no conflict of interest.

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Author Contribution

Yang Yang: drafted this manuscript. Cheng Cheng, XueZhong Dai: Article Design. GuoNing Yang , LiMing Cui , Ma Ya, LiHua Cun , JingYan Duan: improved the structure of this manuscript and completed the diagrams. LiPing Li, QuPing Yuan: manuscript revision. XiangPing Yan: collect information.

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Not Applicable

Data Availability

The datasets analyzed during the current study are available from the corresponding author upon reasonable request. The transcriptomic datasets used in this study were obtained from publicly available databases, including TCGA and GTEx. Due to ethical restrictions and privacy considerations related to the clinical specimens involved in this study, the raw clinical data and original experimental materials are not publicly available. All data supporting the findings of this study are included in the article and its supplementary information files.

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Figures

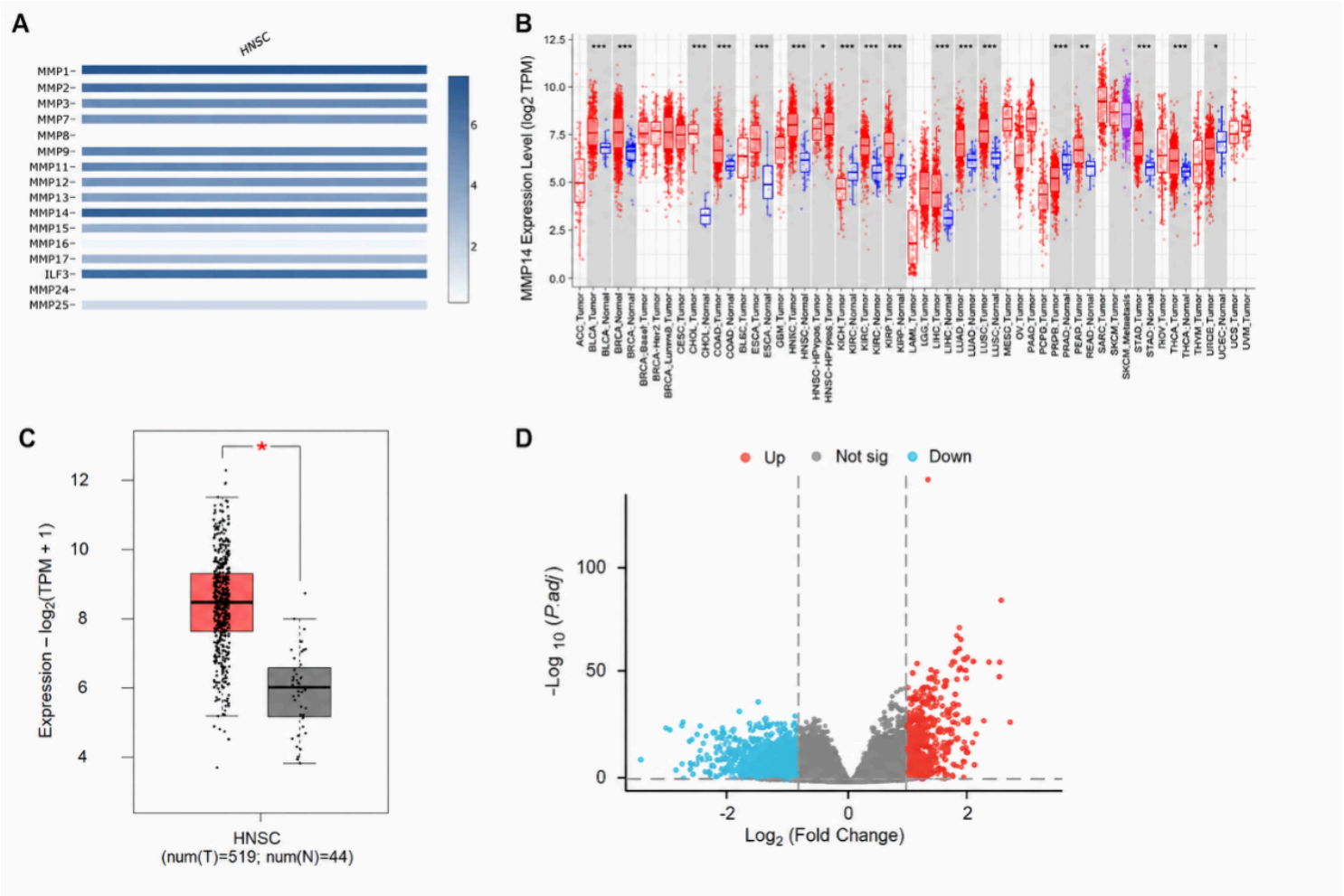


Figure 1

Expression Analysis of MMP14 in HNSCC.**A** The expression of the MMP family in HNSCC within the TCGA database. **B** The expression of MMP14 in various malignant tumors. *P < 0.05 **P < 0.01 ***P < 0.001. **C** The expression of MMP14 in HNSCC tissues compared to normal tissues. **D** The differential expression of the high and low MMP14 gene groups in HNSCC.

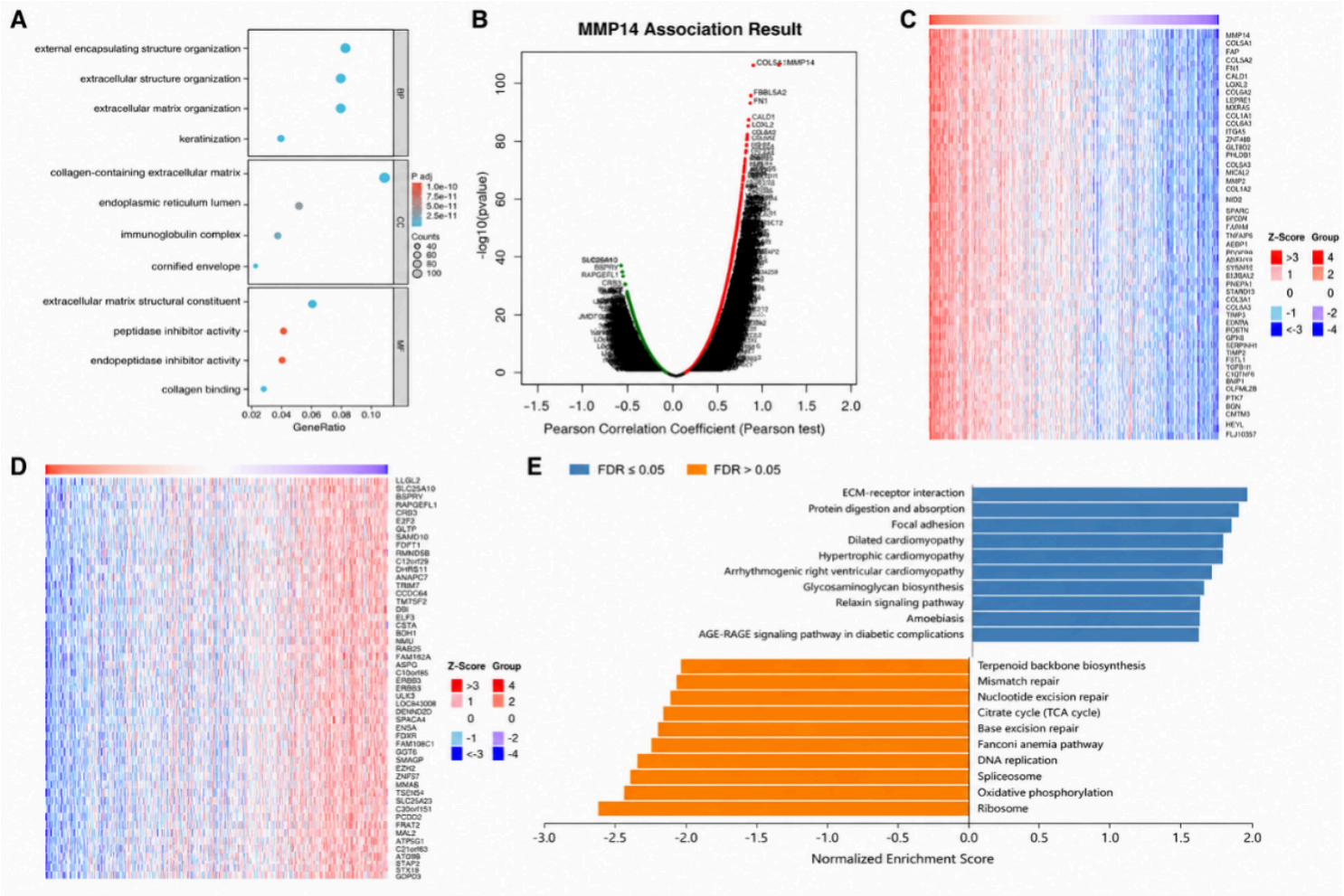


Figure 2

Functional enrichment and pathway analysis of MMP14-related genes. **A** GO enrichment analysis of MMP14-related genes. **B** Pearson correlation analysis of MMP14 and total gene expression in HNSCC. **C** Heatmap of representative gene expressions significantly correlated with MMP14. **D** Heatmap of representative gene expressions significantly negatively correlated with MMP14. **E** GSEA results of the high and low expression groups of MMP14.

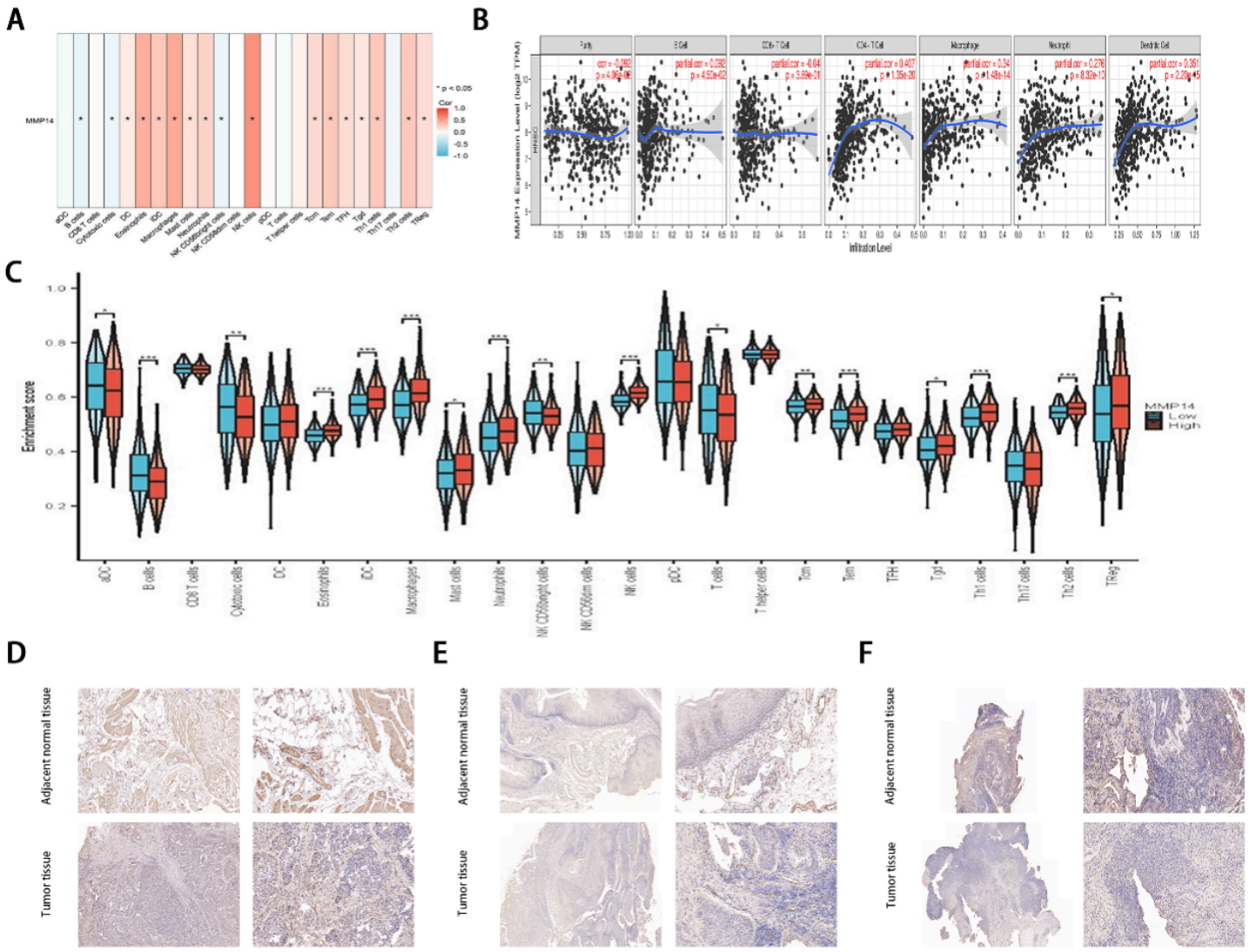


Figure 3

Association of MMP14 expression with immune cell infiltration and immunohistochemical validation in HNSCC. **A**Association between MMP14 expression and immune cell infiltration levels in HNSCC. **B** Relationship between MMP14 expression and the abundance of major immune cell populations. **C** Comparison of immune cells enrichment in high and low MMP14 expression groups. **D-F** Immunohistochemical analysis of HNSCC tissue compared to adjacent non-cancerous tissues.

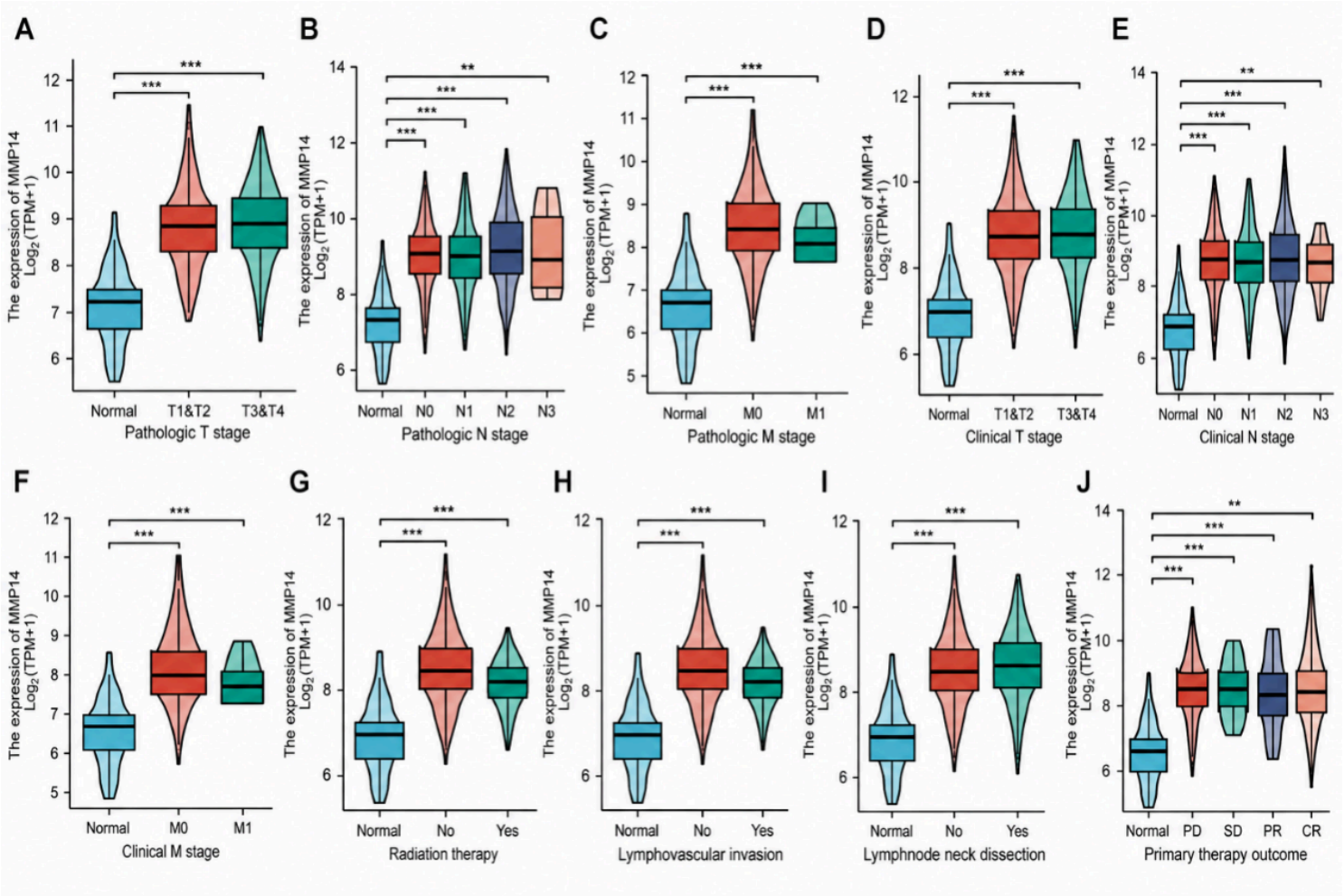


Figure 4

Analysis of MMP14 expression and clinical pathological characteristics of HNSC. **A**Pathological T stage. **B** Pathological N stage. **C** Pathological M stage. **D** Clinical T stage. **E** Clinical N stage. **F** Clinical M stage. **G** Radiotherapy status. **H** Lymphatic vessel invasion. **I**Neck lymph node dissection status. **J** Initial treatment response.

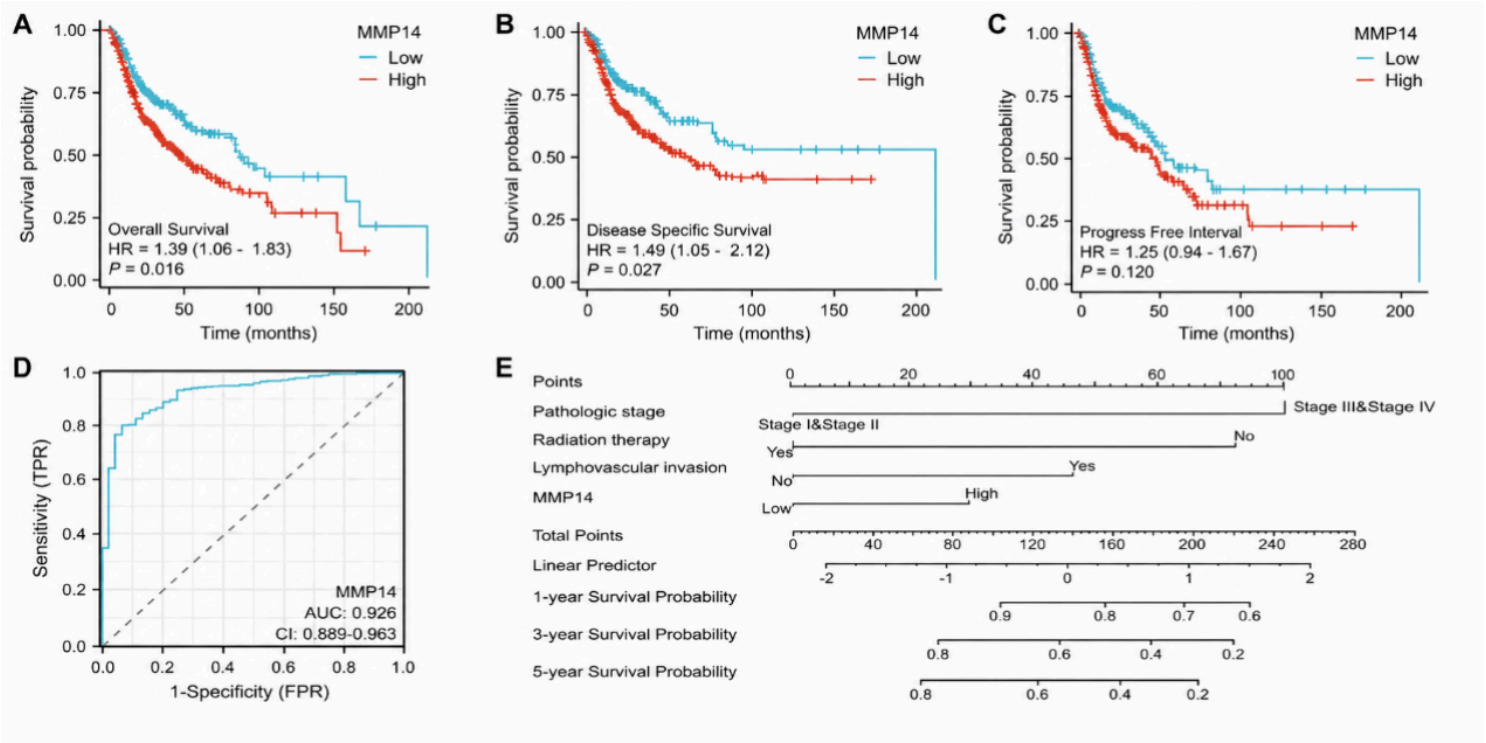


Figure 5

The prognostic value of MMP14 in HNSCC and the construction of a predictive model. **A**Kaplan–Meier overall survival (OS) analysis. **B** Kaplan-Meier disease-specific survival (DSS) analysis. **C** Kaplan-Meier progression-free interval (PFI) analysis. **D** ROC curve evaluation of MMP14's diagnostic value for HNSCC. **E** Construction of a prognostic nomogram to predict survival rates.