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ORIGINAL RESEARCH

Clinicopathological Features and Prognostic Factors of Renal Cell Carcinoma in Young Patients Under 45 Years: A Single-Center Retrospective Study

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Objective: To explore the clinicopathological characteristics, diagnostic approaches, and therapeutic strategies for renal cell carcinoma (RCC) in young patients under 45 years of age, aiming to provide insights for early detection and improved prognosis.

Methods: We retrospectively analyzed the clinical data of 150 RCC patients aged 18 to 45 years treated at the General Hospital of Ningxia Medical University from 2011 to 2023. Clinicopathological features, surgical outcomes, and long-term follow-up data were evaluated.

Results: The study included 82 males and 68 females, with a mean age of 38.89 ± 5.56 years. Clear cell RCC was the most common subtype (72.6%), followed by chromophobe RCC (12%) and papillary RCC (4%). Other rare subtypes included XP11.2 translocation/TFE3 gene fusion - associated RCC (2.7%) and collecting duct RCC (0.7%). In terms of clinical staging, 89% of patients were classified as T1 stage. Follow - up data, ranging from 12 to 153 months, showed that 11 patients died of the disease and 14 exhibited metastasis. Postoperative glomerular filtration rate (GFR) and serum creatinine (CREA)) levels were lower than preoperative levels, and patients who underwent radical nephrectomy (RN) had worse renal function than those who underwent partial nephrectomy (PN). The 3 - year and 5 - year survival rates for the asymptomatic group were 100% and 97%, respectively, while for the symptomatic group, they were 94% and 83%, respectively. Single - factor Cox regression analysis revealed that symptoms, hypertension, clinical stage, pathological grade, and pathological type were independent risk factors for overall survival in young renal cancer patients.

Conclusion: Young RCC patients present with unique clinicopathological characteristics and prognostic factors. Although the overall prognosis is relatively favorable, rare subtypes such as XP11.2 translocation/TFE3 gene fusion - associated RCC and collecting duct RCC are associated with worse outcomes. Early detection through regular physical examinations and prompt treatment are crucial for improving outcomes. PN should be prioritized when feasible, and effective management of comorbidities like hypertension is essential.

Keywords: young patients, renal cell carcinoma, clinical features, pathological features, prognosis

Introduction

RCC is the most common type of kidney cancer, accounting for approximately 90% of all renal malignancies. It is more prevalent in men than in women, with a male-to-female incidence ratio of up to 1.5:1.[1] RCC typically peaks in incidence between the ages of 60 and 70,[2] and is relatively rare in individuals under 40 years old.[3] However, recent studies have shown an increasing incidence of RCC in younger populations.[4]

In younger patients, RCC often presents with distinct clinical and pathological features compared to older patients.[5–7] For instance, younger individuals are more likely to have localized disease at diagnosis, resulting in a better prognosis.[4] Additionally, chromophobe RCC is more prevalent in younger patients, while clear cell RCC remains the most common

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subtype overall.[4] Despite these observations, there remains limited and conflicting data regarding the clinical characteristics and treatment patterns of RCC in young patients.[4]

Current research on the pathogenesis of RCC has identified genetic alterations, such as mutations in the Von Hippel-Lindau (VHL) gene, as significant factors in its development.[2] However, the biological behavior and prognosis of RCC in younger individuals are still not well understood.[8] This study aims to investigate the clinicopathological characteristics and prognosis of RCC in patients under the age of 45, providing valuable insights for urologists in the diagnosis and treatment of this unique subgroup.

Materials and Methods

The study has obtained approval from the ethics committee of our institution. Given that it is a purely retrospective study, the basic information of the patients has been de-identified to ensure robust protection of their privacy. Furthermore, the ethics committee has granted a waiver for informed consent from the patients, in accordance with the nature of the study.

This study retrospectively analyzed the case data of 150 renal cancer patients under the age of 45 who were admitted to the General Hospital of Ningxia Medical University between January 2011 and January 2023. The pathological data of these patients were systematically reviewed, encompassing tumor size, pathological type, stage, grade, and other relevant pathological characteristics. Tumor grading was performed using the 2012 WHO/ISUP grading system,[9] and staging was based on the TNM classification system of the American Joint Committee on Cancer (AJCC) from 2017.[10] In addition, we collected data on patients' smoking history, changes in renal function indices before and after surgery, tumor treatment methods, and other clinicopathological information. Tumor recurrence was defined as the emergence of a new renal malignant tumor at the original site or at other locations following surgical intervention.

The screening criteria for the study are as follows:

Inclusion Criteria

i Patients with complete clinical medical records, pathological diagnosis, and follow-up data; ii Patients who meet the diagnostic criteria for renal cell carcinoma as defined by the World Health Organization; iii Patients whose renal cell carcinoma diagnosis is confirmed through postoperative pathological examination; iv Patients who have undergone surgery performed by chief physicians with over 10 years of experience in similar laparoscopic procedures.

Exclusion Criteria

i Patients with evidence of distant metastasis identified through preoperative imaging or clinical assessment, or those with co-existing malignant tumors in other organs; ii Patients with severe impairments of cardiac, hepatic, or renal function; iii Patients with systemic infections or autoimmune diseases; iv Patients in an extremely fragile condition were unable to tolerate the physical demands and trauma associated with the operation.

Clinical Data

A total of 150 patients were included in this study, comprising 82 males and 68 females, with a male-to-female ratio of 1.2:1. The age range was from 19 to 45 years, with a mean age of 38.89 ± 5.56 years. Upon admission, all patients underwent urinary ultrasound, computed tomography urography (CTU), renal arteriovenous computed tomography, GFR and serum CREA assessments. Based on the presence or absence of clinical symptoms, patients were categorized into symptomatic and asymptomatic groups. The symptomatic group included 35 patients (23%), while the asymptomatic group comprised 115 patients (77%). Initial symptoms among symptomatic patients included gross hematuria of varying degrees in 8 patients, lumbago and abdominal pain in 25 patients, an abdominal mass in 1 patient, and urinary tract infection in 1 patient. The remaining patients were diagnosed incidentally during routine physical examinations. The distribution of renal cancer was 79 cases (57%) on the left side and 71 cases (43%) on the right side. CTU examination revealed no abnormalities in the bladder or ureter for all patients. Complete past medical history data were obtained for each patient. In terms of clinical staging, 133 patients (89%) were classified as Stage T1, 9 patients (6%) as Stage T2, 7 patients (4%) as Stage T3, and 1 patient (1%) as Stage T4. Regarding surgical treatment, 68 patients (45%) underwent RN, and 82 patients (55%) underwent PN. Among the patients, 26 had a history of smoking, with a smoking duration

Table 1 Analysis of Clinicopathological Signs of Symptomatic and Asymptomatic RCC Patients

Variable		Clinical Presentation (n=150)		*P*
		Symptomatic	Asymptomatic	
Gender	Male	20	62	0.737
	Female	15	53	
Average age (years)	38.89±5.56			–
Smoking	No	29	96	0.636
	Yes	6	19	
Tumor side	Left	18	60	0.832
	Right	17	54	
	Bilateral	0	1	
Hypertension	No	25	101	0.021
	Yes	10	14	
Diabetes	No	32	113	0.049
	Yes	3	2	
Mean tumor size (cm)		4.51±2.36	3.63±1.99	–
Tumor size	≥4	18	46	0.231
	<4	17	69	
Surgical modality	RN	25	44	0.001
	PN	10	71	
Clinical stage	Stage I	25	101	0.024
	Stage II	2	3	
	Stage III	4	4	
	Stage IV	4	7	
T stage	T1	28	105	0.049
	T2	2	6	
	T3	3	4	
	T4	2	0	
Histopathology	Clear cell RCC	22	87	0.137
	Chromophobe RCC	5	13	
	Papillary RCC	1	5	
	Other types of RCC	7	7	
	Other types of kidney cancer	0	3	
Pathological grade	WHO grade 1 and 2	21	84	0.334
	WHO grade 3	5	12	
	Other	9	19	

ranging from 7 to 30 years and an average daily consumption of approximately 15 cigarettes. One patient had a family history of renal cancer, and one patient had bilateral renal cancer. The detailed clinicopathological data of the patients are presented in Table 1.

Statistical Analysis

All data were analyzed using R 4.4.1 and SPSS 26.0 software. Continuous variables with a normal distribution were presented as mean ± standard deviation, and intergroup comparisons were performed using the *t*-test for two groups or one-way analysis of variance (ANOVA) for multiple groups. For paired samples across different groups, repeated measures ANOVA was employed. Variables with non-normal distributions were compared using the Wilcoxon rank-sum test for two groups or the Kruskal–Wallis test for multiple groups. Categorical variables were expressed as frequencies and percentages, and analyzed using Fisher's exact test or Pearson's chi-square test, as appropriate. Kaplan-Meier survival curves were generated using the "survminer" package in R 4.4.1 software, and statistical differences were assessed using the Log rank test. All statistical analyses were conducted as two-sided tests, with a significance level set at $P < 0.05$.

Results

Pathological results

All 150 patients underwent postoperative pathological examination, confirming the diagnosis of renal malignant tumors (Table 1). Clear cell RCC was the most prevalent subtype, accounting for 109 cases (72.6%) among both male and female patients. Other subtypes included chromophobe RCC in 18 cases (12%), papillary RCC in 6 cases (4%), multilocular cystic RCC in 6 cases (4%), XP11.2 translocation/TFE3 gene fusion-associated RCC in 4 cases (2.7%), mixed RCC in 3 cases (2%), renal neuroendocrine tumor in 2 cases (1.3%), renal collecting duct carcinoma in 1 case (0.7%), and nephroblastoma in 1 case (0.7%). Pathological grading revealed 24 cases of WHO grade I, 71 cases of WHO grade II, 12 cases of WHO grade III, and 2 cases of G2 carcinomas. In terms of clinical staging, 126 patients were classified as stage I, 5 as stage II, 8 as stage III, and 11 as stage IV. TNM staging showed 133 cases in stage T1, 9 in stage T2, 7 in stage T3, and 1 in stage T4. Notably, one patient had bilateral renal cancer, with chromophobe RCC on the left side and clear cell RCC on the right side. Compared with the asymptomatic group, the symptomatic group had statistically significant differences in the presence of hypertension, diabetes, clinical stage, T-stage, and the proportion of RN versus PN ($P < 0.05$).

Follow-up

All patients were followed up, with a follow-up duration ranging from 12 to 153 months and a mean follow-up time of 66.32 ± 40.958 months. During this period, 11 patients succumbed to the disease, with survival times ranging from 51 to 84 months. The causes of death were attributed to the following histological subtypes: clear cell RCC in 6 cases, XP11.2 translocation/TFE3 gene fusion-associated RCC in 3 cases, papillary RCC in 1 case, and renal collecting duct carcinoma in 1 case. Additionally, 14 patients exhibited varying degrees of metastasis, involving the perirenal space, bone, lung, liver, and peritoneum. Venous tumor thrombus was identified in 2 patients, corresponding to an incidence rate of 1.3%. During postoperative follow-up surveillance, metastatic disease was detected in 12 patients, with metastatic sites including lymph nodes, bone, liver, lungs, and brain. Based on the individual metastatic profiles, targeted adjuvant therapies were administered, comprising palliative radiotherapy and targeted pharmacotherapy.

Prognosis

Through the comparison and analysis of glomerular filtration rate (GFR) and serum creatinine levels before and after surgery, we observed that postoperative GFR and serum creatinine levels were lower than preoperative levels. Additionally, patients who underwent RN exhibited worse renal function compared to those who underwent PN (Table 2). During the follow-up period, 10 patients died due to tumor recurrence and metastasis, while one patient died from non-tumor-related causes. At 3 years, 148 patients were still alive, corresponding to a survival rate of 98.6%; at 5 years, 144 patients remained alive, with a survival rate of 94%. For the asymptomatic group, the 3-year and 5-year survival rates were 100% and 97%, respectively, while for the symptomatic group, these rates were 94% and 83%, respectively. The 3-year and 5-year survival rates of the symptomatic group were significantly lower than those of the asymptomatic group.

Table 2 Comparative Analysis of Renal Function Before and After Surgery in Patients with RCC

Variable	Clinical Presentation		*P*	Surgical Methods		*P*
	Symptomatic	Asymptomatic		RN	PN	
Pre-GFR(mL/min/1.73m2)	110.4±32.18	115.82±25.74	0.358	108.67±28.27	119.71±25.62	0.032
P-GFR(mL/min/1.73m2)	72.97±24.89	89.53±28.2	0.001	67.86±19.67	101.26±25.62	<0.001
Pre-CREA(μmol/L)	94±150.28	66.61±18.97	0.137	82.5±107.79	64.68±13.99	0.136
P-CREA(μmol/L)	124.85±159.09	81.19±29.5	0.003	118.83±114.18	75.99±19.42	<0.001

Abbreviations: Pre-GFR, Pre-operative GFR; P-GFR, Post operative GFR; Pre-CREA, Pre - operative serum creatinine level; P-CREA, Post-operative serum creatinine level.

Table 3 Univariate Cox Regression Analysis Affecting Postoperative OS in Patients with RCC

Variable	Single Factor	
	HR (95% CI)	P
Symptoms (No/Yes)	5.374 (1.558~18.536)	0.008
Gender (M/F)	2.683(0.710~10.143)	0.146
Smoking (No/Yes)	0.496(0.178~1.388)	0.142
Tumor size (<4cm/≥4cm)	0.190(0.041~0.878)	0.034
Hypertension (No/Yes)	8.612(2.517~29.467)	0.001
Diabetes mellitus (No/Yes)	0.601(0.216~1.668)	0.328
Tumor side (left/right/bilateral)	0.506(0.146~1.751)	0.282
Surgical Approach (RN/PN)	8.316(1.058~65.393)	0.044
Clinical stage (stage I./II./III./IV.)	3.403(1.961~5.905)	<0.001
T-staging (T1/T2/T3/T4)	1.964(1.156~3.337)	0.013
Type of pathology	15.636(2.579~94.764)	0.003
Pathologic grade (WHO1 and 2/WHO3/other)	0.216(0.047~0.989)	0.043

Abbreviations: M, Male; F, Female; HR, Hazard Ration; CI, Confidence Interval.

The results of the single-factor Cox regression analysis related to prognosis are presented in Table 3. This analysis identified symptoms, hypertension, clinical stage, pathological grade, and pathological type as independent risk factors for overall survival (OS) in young renal cancer patients ($p<0.05$). Additionally, several key findings emerged: Our study revealed that patients with AJCC stage I and II disease had high survival rates, whereas those with stage III and IV disease exhibited significantly lower survival rates (Figure 1). Significant differences in survival rates were also observed among different pathological types, with particularly poor survival outcomes noted for other types of renal malignancies, such as collecting duct carcinoma and XP11.2 translocation/TFE3 gene fusion-associated RCC (Figure 2). Additionally, patients with clinical symptoms had significantly higher survival rates compared to those without symptoms (Figure 3). The survival rate for patients undergoing laparoscopic radical resection was significantly lower than that for those undergoing PN (Figure 4). Furthermore, our study found that patients with hypertension had lower survival rates compared to those without hypertension (Figure 5).

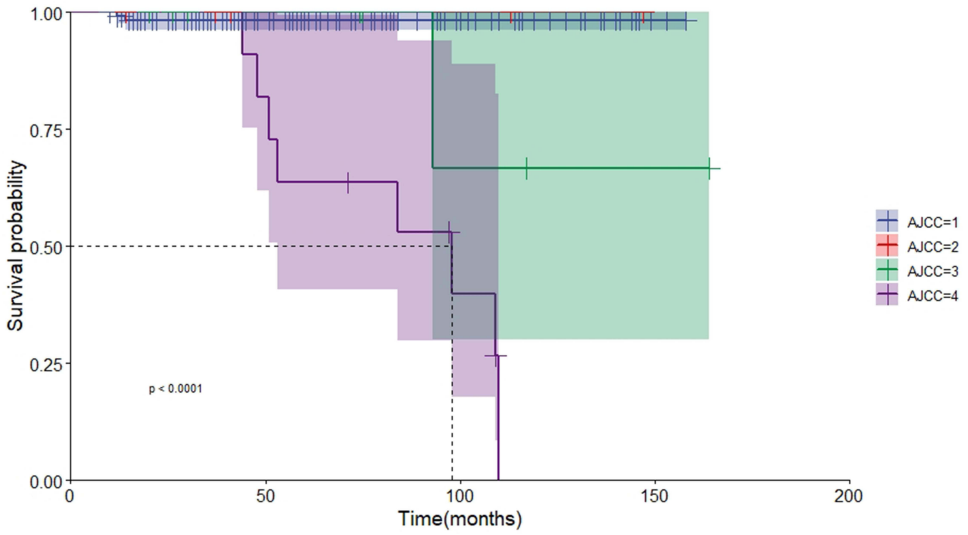

Figure 1 Survival analysis of patients with RCC at different AJCC clinical stages. 1 - AJCC stage I, 2 - stage II, 3 - stage III, and 4 - AJCC stage IV.

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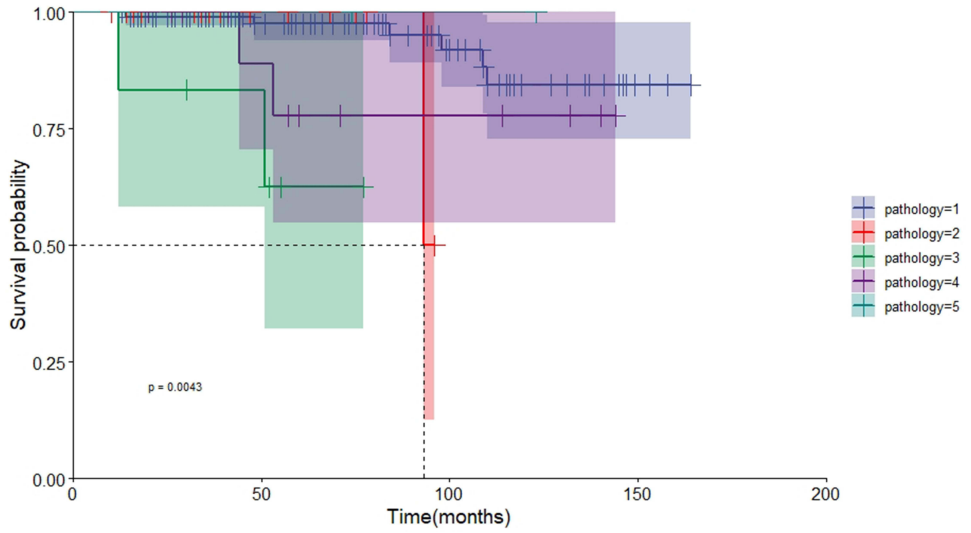

Figure 2 Survival analysis of patients with different pathological types of RCC. 1 - Clear cell RCC; 2 - Chromophobe RCC; 3 - Papillary RCC; 4 - Other types of RCC; 5 - Represents other types of renal malignancies.

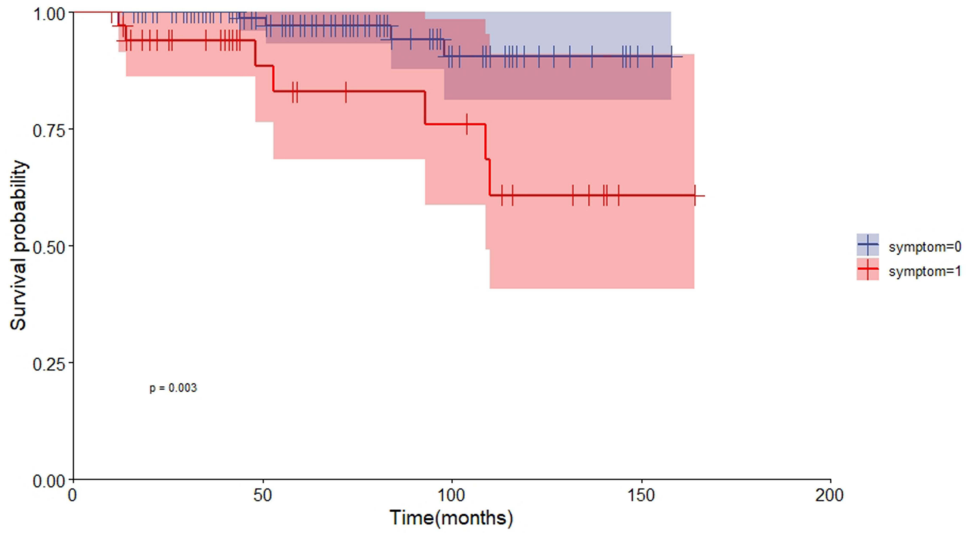

Figure 3 Survival rate analysis of patients with RCC with clinical symptoms. 1 - symptomatic group; 0 -asymptomatic group.

Discussion

In young patients, the clinical and pathological features of RCC often diverge significantly from those observed in their elderly counterparts. Emerging evidence indicates that RCC patients under 40 years of age typically present with more favorable tumor profiles. Specifically, these tumors tend to be localized, and the incidence of metastasis remains relatively low.[4] Notably, young RCC cohorts demonstrate a higher proportion of female patients, accompanied by an increased prevalence of oncocytoma as the predominant pathological subtype. With respect to histological classification, non-clear cell carcinomas, including oncocytoma and papillary carcinoma, are disproportionately represented among younger patients.[11] Collectively, these findings suggest that young RCC patients may exhibit distinct disease manifestations and underlying biological behaviors compared to elderly patients, highlighting the need for age - specific management strategies.

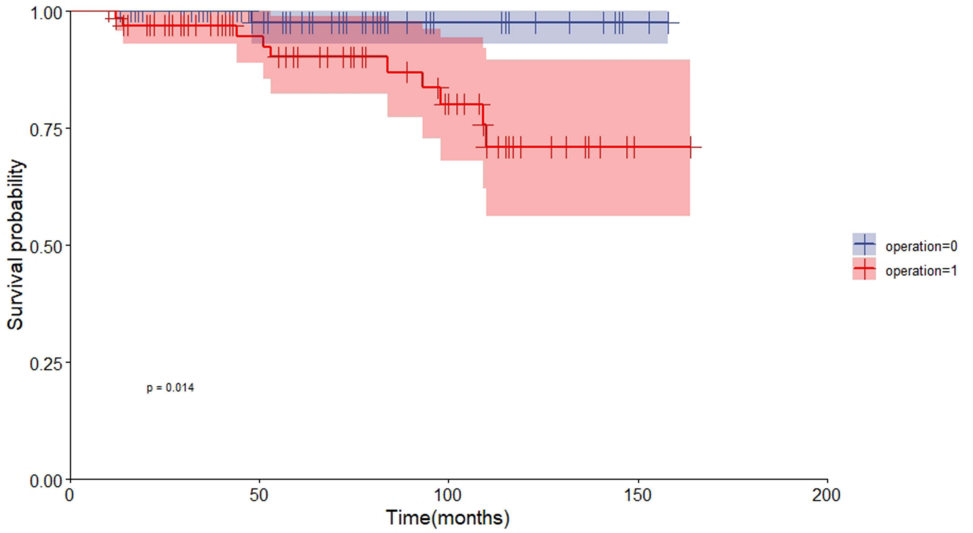

Figure 4 Survival analysis of patients with RCC undergoing RN and PN. 0 - PN,1 - RN.

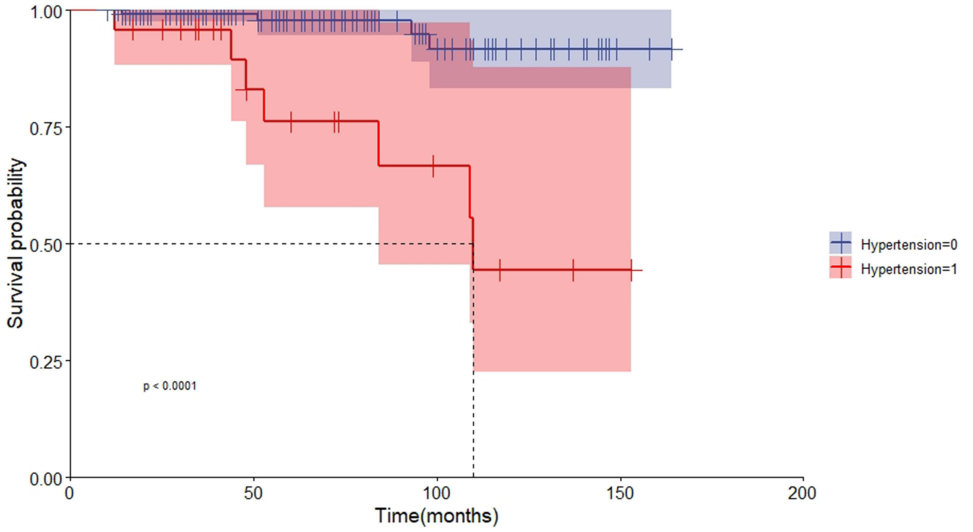

Figure 5 Survival analysis of patients with RCC complicated with hypertension. 1 - hypertension, 0 - no hypertension.

The findings of this study offer substantial insights into RCC among young patients under the age of 45, providing insights into its clinicopathological characteristics, prognosis, and treatment strategies. Our study shows that young RCC patients accounted for 8.7% of all RCC cases in our hospital, aligning with previous reports indicating that RCC in patients younger than 45 years represents approximately one - tenth of all RCC cases.[12] Clear cell RCC was the most predominant subtype (72.6%) in our cohort, consistent with its prevalence as the most common subtype overall in RCC.[13] However, the proportion of chromophobe RCC (12%) being higher than papillary RCC (4%) in young patients differs from some previous studies. For example, Taha et al and Muhammed et al reported papillary RCC as the predominant non - clear cell RCC subtype in young patients.[14,15] These discrepancies may be attributed to geographical and ethnic variations. Different regions may have distinct genetic backgrounds and environmental exposures, which can influence the development and distribution of RCC subtypes.

We identified several rare cases of RCC, including the XP11.2 translocation/TFE3 gene fusion-associated RCC subtype. This subtype is predominantly observed in children, accounting for 20–40% of pediatric RCC cases, while its incidence in adults is exceedingly rare, representing only 1–1.6% of all renal tumors.[16] Research has shown that pediatric

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patients with this subtype often exhibit indolent disease progression, whereas adult patients typically present with aggressive disease, metastasis, and shorter overall survival periods.[17,18] Additionally, its incidence is higher in females than in males,[19] and it is associated with a high metastasis rate and poor prognosis.[20,21] In our cohort, XP11.2 translocation/TFE3 gene fusion-associated RCC accounted for 2.7% of cases, primarily affecting young females (3 females and 1 male), with the oldest patient being 33 years old. Notably, symptomatic patients within this group exhibited significantly better prognoses compared to asymptomatic patients. However, given the small sample size, the impact of symptoms on prognosis in XP11.2 translocation/TFE3 gene fusion-associated RCC warrants further investigation. Among these cases, three exhibited distant metastases of varying degrees postoperatively, and one had a vascular tumor thrombus, highlighting the significantly worse prognosis, higher metastasis rate, and shorter OS compared to other RCC subtypes in young renal cancer patients. Collecting duct RCC has been demonstrated that it often presents at advanced stages and is associated with poor outcomes.[22] Andrea et al[23] reported that the survival rate for stage IV collecting duct carcinoma is extremely low, with a median cancer-specific survival of only 18 months. RN combined with systemic therapy is the primary treatment approach, with both modalities showing significant protective effects. In our study, we identified one case of collecting duct carcinoma in a patient under 45 years old, who presented with persistent gross hematuria for over two months. The tumor was staged as T4N1M1 (stage IV), with a size of 9.5 cm. The patient underwent left RN, and pathology confirmed collecting duct carcinoma. Postoperatively, the patient received a combination of axitinib and everolimus. After 23 months of follow-up, liver metastasis was detected, and by 48 months, multiple metastases, including bone and lung metastases, were observed. This case underscores the low survival rate of collecting duct carcinoma in young patients. However, the survival period following RN and systemic therapy exceeded the median cancer-specific survival reported in previous studies. Due to the limited number of collecting duct carcinoma cases in our study, further research with larger sample sizes is needed to better understand its incidence and prognosis in young patients.

Many young RCC patients exhibit no obvious symptoms in daily life, with lesions often discovered incidentally during routine physical or imaging examinations. In our study, 115 patients were asymptomatic, with renal tumors detected during physical examinations and subsequently confirmed as renal malignancies postoperatively, significantly outnumbering the symptomatic group (35 cases).

Smoking and hypertension are established risk factors for RCC, with most patients having associations with these factors.[24] Studies have shown that hypertension may affect the prognosis of patients with renal cancer by causing vascular endothelial dysfunction, activating the renin-angiotensin system, and altering the tumor microenvironment.[25] In our study, hypertension remained a significant risk factor for RCC in young patients, while smoking did not show a clear association. The possible mechanisms of the impact of hypertension on the prognosis of young patients with RCC still require further study in the future.

Locally advanced RCC usually has a large tumor volume (stage T3 or T4) and may invade the perirenal fat, venous system or adjacent organs. These characteristics increase the complexity of the surgery and the difficulty of complete resection, leading to a higher risk of postoperative recurrence and metastasis.[26] For young patients, the presence of typical clinical symptoms often suggests advanced disease or a higher clinical stage, which is associated with a poorer prognosis. In accordance with clinical guidelines, these patients are generally recommended to undergo RN. Several studies have consistently demonstrated that RN and PN yield comparable outcomes in terms of OS and cancer-specific survival.[27]

In our study, we found that patients with advanced stages, clinical symptoms, and those who underwent RN had worse prognoses compared to the control group, primarily due to the relatively late clinical stage. Our results also demonstrated that RN has a more pronounced impact on renal function than PN. This study does have some limitations. The relatively small sample size and single-center design may limit the statistical power of the results. Nevertheless, the findings of this study are still highly relevant and merit significant attention from urologists.

For young patients with postoperative pathology suggesting XP11.2 translocation/TFE3 gene fusion-associated RCC or collecting duct RCC, we recommend prompt genetic testing and standardized treatment to improve prognosis and quality of life.

This study is subject to several limitations. As a single - center, retrospective study, it's prone to selection bias, which affects the findings' validity and limits their broader applicability. Also, the small sample sizes for rare RCC subtypes make it hard to draw conclusions about their management and prognostic factors. Future research should focus on multi - center collaborations to gather a larger, more diverse patient cohort, enhancing the studies' power. Additionally, collecting long - term follow - up data is essential for better understanding the disease course and outcomes in young RCC patients.

Conclusion

RCC in young patients under 45 years of age represents a unique clinical scenario with distinct clinicopathological characteristics and prognostic implications. While the overall prognosis for this subgroup is generally more favorable than that of older patients, specific rare subtypes, such as XP11.2 translocation/TFE3 gene fusion-associated RCC and collecting duct RCC, are associated with significantly worse outcomes, characterized by high metastasis rates and shorter survival times. Additionally, symptomatic presentation and advanced clinical stage are identified as critical risk factors for poorer prognosis in young RCC patients. Our study highlights the crucial role of early detection through regular physical examinations, particularly focusing on the urinary system, and prompt treatment to improve outcomes. Given the significant impact of surgical approach on renal function and prognosis, PN should be prioritized as a preferred treatment option whenever feasible, especially for patients with localized disease. Moreover, effective management of comorbidities such as hypertension is essential for optimizing long-term survival and quality of life in young RCC patients. In summary, a comprehensive evaluation of clinical, pathological, and surgical factors is essential to optimize management and improve the prognosis for this unique subgroup of young RCC patients.

Ethics Statement

The study complies with the Declaration of Helsinki. This study was approved by the Ethics Committee of the General Hospital of Ningxia Medical University (No. KYLL-2025-0219). As it is a purely retrospective study with no privacy concerns, the committee waived the need for patient informed consent.

Disclosure

The author(s) report no conflicts of interest in this work.

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