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The impact of radiotherapy on the prognosis of metastatic clear cell renal cell carcinoma after surgery

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Clear cell renal cell carcinoma, one of the most common types of renal cell carcinoma, has been increasing in incidence year by year. This study aims to investigate the impact of radiotherapy on the prognosis of patients with metastatic clear cell renal cell carcinoma (mccRCC) undergoing cytoreductive surgery. Clinical data of patients with mccRCC who underwent cytoreductive surgery were collected from the SEER database (2000–2021). This study employed propensity score matching (PSM) and R software to evaluate the overall survival (OS) of radiotherapy. Univariate and multivariate COX regression analyses were conducted to explore the impact of different variables on prognosis. Finally, a nomogram was developed to predict patient survival rates. A total of 2076 patients with mccRCC who underwent cytoreductive surgery were included in this study, with 538 (25.92%) in the radiotherapy group and 1539 (74.08%) in the non-radiotherapy group. After propensity score matching (PSM), there were 300 cases in each group. Kaplan-Meier values and the Cox proportional hazards model were used to plot the overall survival (OS) curves, which showed that the median survival time in the radiotherapy group was significantly lower than that in the non-radiotherapy group. Additionally, multivariate Cox regression analysis revealed that tumor grade, N stage, radiotherapy, lung metastasis, and liver metastasis were independent factors affecting the prognosis of patients with mccRCC undergoing cytoreductive surgery. Lastly, a nomogram was developed to estimate the survival rates of patients with mccRCC after cytoreductive surgery. Radiotherapy after cytoreductive surgery may have an adverse impact on the prognosis of patients with mccRCC.

Keywords Metastatic clear cell renal cell carcinoma, Surgery, Radiotherapy, Propensity score matching, Overall survival

Despite recent advancements in diagnostic and therapeutic techniques, renal cell carcinoma (RCC) remains one of the most common and lethal malignancies of the urinary system[1]. Globally, the incidence of RCC ranks 14th among all malignancies, with the highest rates observed in Europe and North America[2]. Approximately 25–35% of patients are initially diagnosed with metastatic RCC, and their five-year survival rate is only around 12%, significantly lower than the 60% five-year survival rate for non-metastatic patients[3]. Data from 2020 indicates that there are over 140,000 RCC-related deaths annually, with systemic metastasis being the primary cause of death for RCC patients[4].

The treatment of patients with metastatic clear cell renal cell carcinoma (mccRCC) is particularly critical. Traditional treatment methods mainly focus on cytoreductive surgery combined with systemic drug therapy[5]. Po-Yen Hsieh and others found that cytoreductive surgery can maximize tumor resection, improve patients' quality of life, prolong lifespan, and increase survival time[6–8]. However, there is still no unified conclusion on the specific post-surgical treatment plan after cytoreductive surgery. Muhammad Ali and others discovered that radiotherapy can be safely and effectively used to treat mccRCC patients, especially those who cannot tolerate surgery, and the treatment effect is related to the dose of radiotherapy[9,10]. Nevertheless, Bingran Wang et al.'s research seems to contradict this conclusion, suggesting that radiotherapy is not recommended for mccRCC patients, with a five-year survival rate of less than 10%[11]. Therefore, to investigate the impact of radiotherapy after cytoreductive surgery on the prognosis of mccRCC patients, this study conducted a comprehensive analysis using the SEER database to compare their survival rates.

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Methods

Patients selection

All patient cases in this study were sourced from the SEER database (https://seer.cancer.gov/), which records basic information about cancer patients in the United States, including age, gender, race, marital status, tumor size, tumor grade, TNM staging, metastasis, treatment methods, survival status, and survival time[12]. Using SEER*Stat software (version 8.4.4), we extracted data on 276,265 kidney cancer patients from the SEER database spanning from 2000 to 2020.

Initially, we retained 133,167 cases of clear cell renal cell carcinoma (ccRCC). Among these, 121,794 patients underwent surgical treatment. Specifically, 2,312 patients were in the M1 stage, indicating distant metastasis. We further screened these 2,312 surgically treated mccRCC patients using the following exclusion criteria (Fig. 1): (1) unknown or unmeasurable tumor size ($n=80$); (2) T-stage could not be assessed ($n=26$); (3) N-stage could not be assessed ($n=113$); (4) unknown race ($n=5$); (5) unknown bone metastasis ($n=33$); (6) unknown brain metastasis ($n=43$); (7) unknown liver metastasis ($n=36$); (8) unknown lung metastasis ($n=41$). Finally, we identified data for 2,076 eligible surgically treated mccRCC patients.

Study variables

The variables included in this study are age, gender, race, marital status, tumor size, tumor grade, radiotherapy, chemotherapy, metastasis to lungs, liver, bones, and brain, survival status, and survival months. Next, we grouped these variables. Firstly, age was categorized into two groups: <60 years and ≥60 years, with 60 years as the cutoff. Race was divided into three groups: White, Black, and Other. The "Other" group included "Asian or Pacific Islander" and "Asian or Pacific Islander". Marital status was defined as married or single/unknown, where "separated/divorced", "single", and "widowed" were all grouped under "single/unknown". Due to the small number of patients in the well-differentiated grade I tumor group, tumor grades were classified into four categories: well or moderately differentiated I/II, poorly differentiated III, undifferentiated IV, and other. Additionally, tumor size was categorized into two groups based on a cutoff of 7 centimeters: <7 cm and ≥7 cm. Both radiotherapy and chemotherapy were classified as "yes" or "no/unknown". The radiotherapy group included "beam radiation", "radiation, NOS (method or source not specified)", and "radioactive implants", with almost all patients receiving "beam radiation".

Statistical analysis

Firstly, this study divided the mccRCC patients undergoing surgery into two groups: those who received radiotherapy and those who did not, with all patients receiving routine systemic therapy postoperatively. A 1:1 propensity score matching (PSM) was employed to minimize selection bias and potential confounding factors between the two groups, with a P-value > 0.05 indicating that we had roughly balanced the influence of these factors. Subsequently, we used Kaplan-Meier curves to examine the overall survival (OS) of patients with mccRCC treated surgically and analyzed differences between the curves using the log-rank test. Furthermore, we conducted subgroup analyses for patients with metastases in different locations to examine the prognostic impact of radiotherapy on surgically treated ccRCC with metastases in various sites. Next, we utilized a univariate model to analyze prognostic factors associated with surgically treated mccRCC, incorporating variables with a p-value < 0.05 into a multivariable Cox model to further identify independent prognostic factors and measure hazard ratios (HR) and 95% confidence intervals (CI). Finally, based on the results of the multivariable Cox proportional hazards regression model, variables with independent prognostic influence were selected to construct a prognostic nomogram for mccRCC patients treated surgically, predicting the survival rate of each patient.

Results

Study cohort selection and propensity score matching

We screened a total of 276,265 patients with RCC from the SEER database and selected them based on inclusion and exclusion criteria, ultimately obtaining information on 2,076 patients with surgically treated mccRCC (Fig. 1). This study employed propensity score matching (PSM) to reduce the impact of selection bias and other potential confounding factors (Table 1). Before PSM, 1,538 patients (74.08%) with mccRCC who underwent surgery did not receive radiotherapy, while 538 patients (25.92%) did. Among the indicators included in this study, age ($p=0.002$), tumor size ($p<0.001$), T stage ($p=0.001$), chemotherapy ($p<0.001$), and metastasis to lungs, liver, bones, and brain ($p<0.001$) were all statistically significant, which may have a critical impact on our discussion. Therefore, we performed 1:1 matching to reduce selection bias and potential confounding factors between the two groups. After PSM, among the surgically treated mccRCC patients, there were 300 patients in the radiotherapy group and 300 patients in the non-radiotherapy group, accounting for 50% each. Age ($p=0.741$), tumor size ($p=0.396$), T stage ($p=0.684$), chemotherapy ($p=0.869$), lung metastasis ($p=0.870$), liver metastasis ($p=0.615$), bone metastasis ($p=0.594$), and brain metastasis ($p=0.483$) - all the indicators we included had p-values > 0.05. Thus, PSM minimized potential confounding factors.

Survival analysis on OS

By comparing the overall survival (OS) between the matched radiotherapy group (300 cases) and the non-radiotherapy group (300 cases), we found that the median survival time for patients receiving radiotherapy was 25 months, whereas it was 31 months for the non-radiotherapy group, showing a statistically significant difference ($p=0.05$) (Fig. 2). This suggests that radiotherapy may lead to poorer prognosis for mccRCC patients who have undergone surgery.

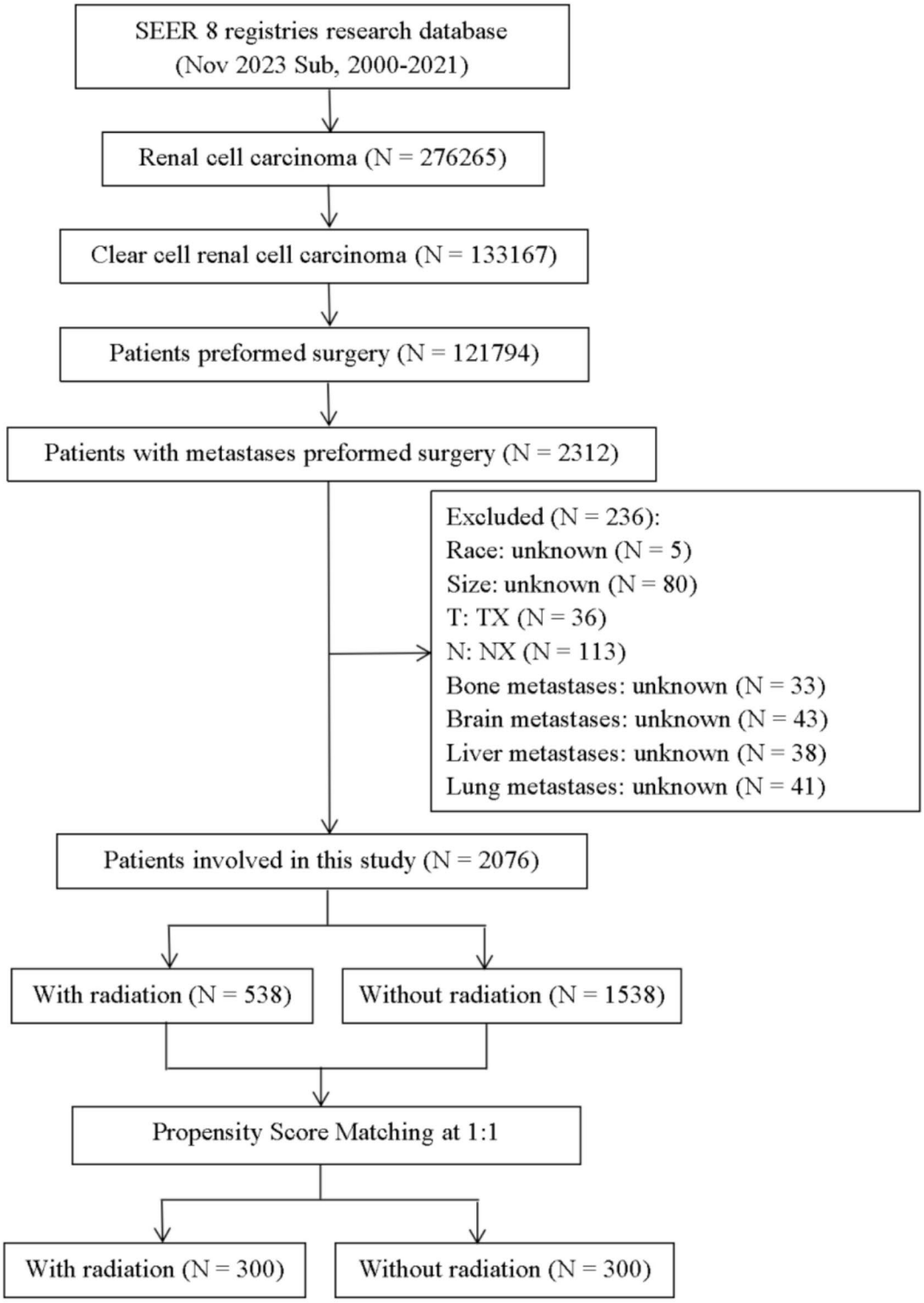

Fig. 1. Flowchart of surgically treated mccRCC patients selection.

Furthermore, we conducted a subgroup analysis of post-surgical mccRCC patients. Based on whether bone metastasis occurred, we discovered that for patients without bone metastasis, the median survival time was 33 months in the non-radiotherapy group and 19 months in the radiotherapy group ($p < 0.05$), indicating statistical significance (Fig. 3). Similarly, when considering brain metastasis, the study found that in the absence of brain metastasis, the prognosis was poorer in the radiotherapy group compared to the non-radiotherapy group, with median survival times of 26 and 31 months, respectively ($p < 0.05$), demonstrating statistical significance (Fig. 4). For patients without liver metastasis, the prognosis was better in the non-radiotherapy group, with median

Variable	Before propensity score matching			After propensity score matching		
	Without radiation (1538)	With radiation (538)	*P*	Without radiation (300)	With radiation (300)	*P*
Age (%)			0.002			0.741
< 60	612 (39.8)	256 (47.6)		129 (43.0)	124 (41.3)	
≥ 60	926 (60.2)	282 (52.4)		171 (57.0)	176 (58.7)	
Sex (%)			0.193			0.465
Male	1070 (69.6)	391 (72.7)		222 (74.0)	213 (71.0)	
Female	468 (30.4)	147 (27.3)		78 (26.0)	87 (29.0)	
Race (%)			0.053			0.754
White	1325 (86.2)	481 (89.4)		267 (89.0)	175 (10.3)	
Black	84 (5.5)	16 (3.0)		15 (5.0)	12 (4.0)	
Other	129 (8.4)	41 (7.6)		18 (6.0)	21 (7.0)	
Marital status (%)			0.098			0.383
Married	1016 (66.1)	377 (70.1)		197 (65.7)	208 (69.3)	
Single/Unknown	522 (33.9)	161 (29.9)		103 (34.3)	92 (30.7)	
Size (%)			< 0.001			0.396
< 7 cm	381 (24.8)	190 (35.3)		103 (34.3)	114 (38.0)	
≥ 7 cm	1157 (75.2)	348 (64.7)		197 (65.7)	186 (62.0)	
Grade (%)			0.117			0.439
Grade I/II	312 (20.3)	111 (20.6)		53 (17.7)	62 (20.7)	
Grade III	597 (38.8)	205 (38.1)		121 (40.3)	102 (34.0)	
Grade IV	466 (30.3)	146 (27.1)		87 (29.0)	94 (31.3)	
Unknown	163 (10.6)	76 (14.1)		39 (13.0)	42 (14.0)	
T (%)			0.001			0.684
T1	203 (13.2)	103 (19.1)		58 (19.3)	65 (21.7)	
T2	208 (13.5)	85 (15.8)		44 (14.7)	37 (12.3)	
T3	971 (63.1)	311 (57.8)		182 (60.7)	178 (59.3)	
T4	156 (10.1)	39 (7.2)		16 (5.3)	20 (6.7)	
N (%)			0.103			0.836
N0	1211 (78.7)	442 (82.2)		244 (81.3)	241 (80.3)	
N1	327 (21.3)	96 (17.8)		56 (18.7)	59 (19.7)	
Chemotherapy (%)			< 0.001			0.869
No/Unknown	778 (50.6)	199 (37.0)		125 (41.7)	128 (42.7)	
Yes	760 (49.4)	339 (63.0)		175 (58.3)	172 (57.3)	
Lung metastasis(%)			< 0.001			0.870
No/Unknown	538 (35.0)	323 (60.0)		159 (53.0)	1219 (71.6)	
Yes	1000 (65.0)	215 (40.0)		141 (47.0)	144 (48.0)	
Liver metastasis(%)			< 0.001			0.615
No/Unknown	1364 (88.7)	512 (95.2)		283 (94.3)	279 (93.0)	
Yes	174 (11.3)	26 (4.8)		17 (5.7)	21 (7.0)	
Bone metastasis(%)			< 0.001			0.594
No/Unknown	1292 (84.0)	166 (30.9)		87 (29.0)	94 (31.3)	
Yes	246 (16.0)	372 (69.1)		213 (71.0)	206 (68.7)	
Brain metastasis(%)			< 0.001			0.483
No/Unknown	1512 (98.3)	411 (76.4)		275 (91.7)	269 (89.7)	
Yes	26 (1.7)	127 (23.6)		25 (8.3)	31 (10.3)	

Table 1. Baseline characteristics of patients before and after PSM.

survival times of 30 and 25 months, respectively ($p < 0.05$), again showing statistical significance (Fig. 5). Finally, we discussed lung metastasis and found that in the group with lung metastasis, the prognosis was better in the non-radiotherapy group, with median survival times of 20 and 16 months, respectively ($p < 0.05$), indicating statistical significance (Fig. 6). Other groups in this study did not show statistical significance, possibly due to the small sample size, as we hypothesize.

Univariate and multivariate analysis

In this study, univariate and multivariate Cox regression analyses were performed on the post-PSM cohort. Based on the results of the univariate Cox regression analysis, tumor size ($p = 0.050$), tumor grade ($p < 0.001$), T stage ($p < 0.001$), N stage ($p < 0.001$), radiotherapy ($p = 0.003$), chemotherapy ($p = 0.002$), lung metastasis ($p < 0.001$),

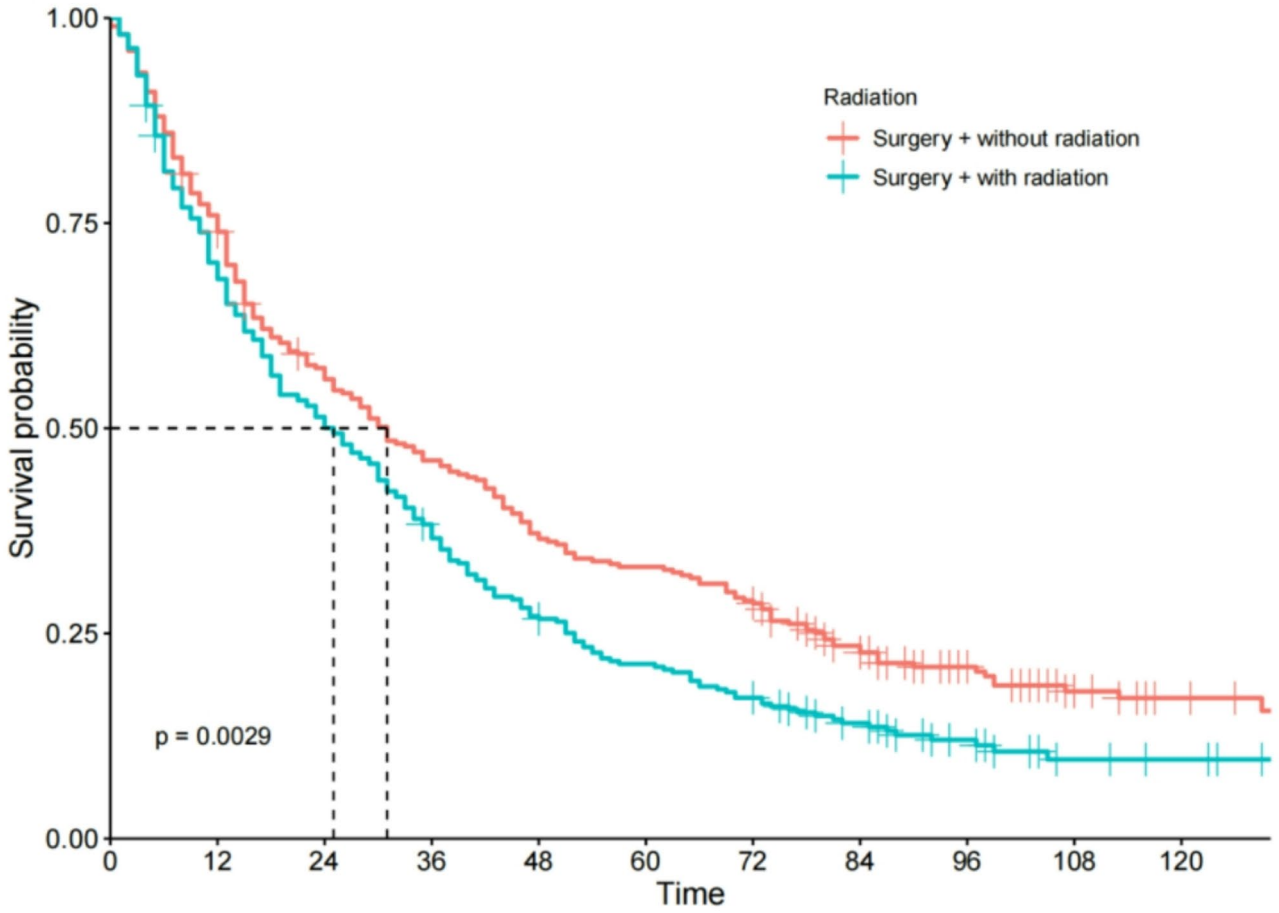

Fig. 2. Survival curve of surgically treated mccRCC patients by radiotherapy.

and liver metastasis ($p = 0.002$) all affected the OS of patients. Consequently, we incorporated these variables into a multivariate Cox model, which revealed that tumor grade ($p < 0.001$), N stage ($p < 0.001$), radiotherapy ($p < 0.001$), lung metastasis ($p = 0.013$), and liver metastasis ($p = 0.035$) independently influenced the survival of surgically treated mccRCC patients (Table 2).

Nomogram construction

Based on the independent factors identified through Cox multivariate regression analysis and their clinical applicability, this study constructed a nomogram (Fig. 7) that incorporates tumor grade, N stage, radiotherapy, lung metastasis, and liver metastasis as variables. Each variable is assigned a corresponding score aligned with the scale at the top of the nomogram. For instance, the administration of radiotherapy is assigned a score of 35. Consequently, by summing up the respective points, we can determine the 1-year, 3-year, and 5-year survival rates.

Discussion

The treatment of patients with mccRCC remains controversial. Muhammad Ali et al. believe that radiotherapy is meaningful and can improve patients' survival time, while Bingran Wang et al. hold the opposite view[9,11,13,14]. Therefore, whether patients can benefit from radiotherapy after cytoreductive surgery has not yet reached a clear conclusion, and research in this area is scarce. Further investigation into the role of radiotherapy in this context remains challenging.

In this study, we used data from the SEER database, which provides information on various tumor patients in the United States to explore the impact of different variables on the survival of tumor patients. We divided patients with mccRCC who underwent cytoreductive surgery into two groups based on whether they received radiotherapy. We found that compared with patients who did not receive radiotherapy, the OS of patients in the radiotherapy group was significantly reduced by approximately 6 months. Subgroup analysis also indicated that radiotherapy might have a negative impact on patients' prognosis. Multivariate Cox regression analysis showed that radiotherapy was an independent harmful factor affecting the prognosis of mccRCC.

The question of whether radiotherapy is necessary for patients with mccRCC undergoing cytoreductive surgery remains ambiguous. However, numerous studies have demonstrated that aggressive multimodal therapy can enhance treatment efficacy and survival outcomes for these patients. In this study, we aimed to investigate

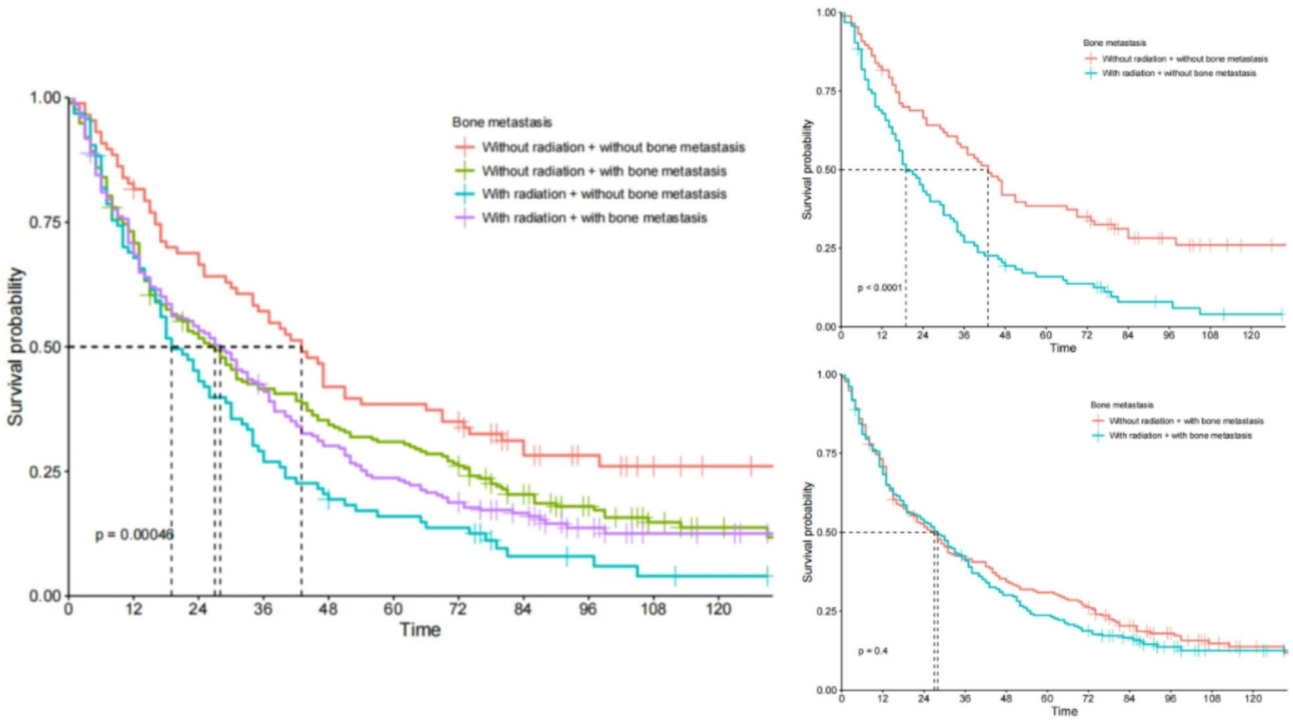

Fig. 3. Survival curve of surgically treated mccRCC patients by radiotherapy and bone metastasis.

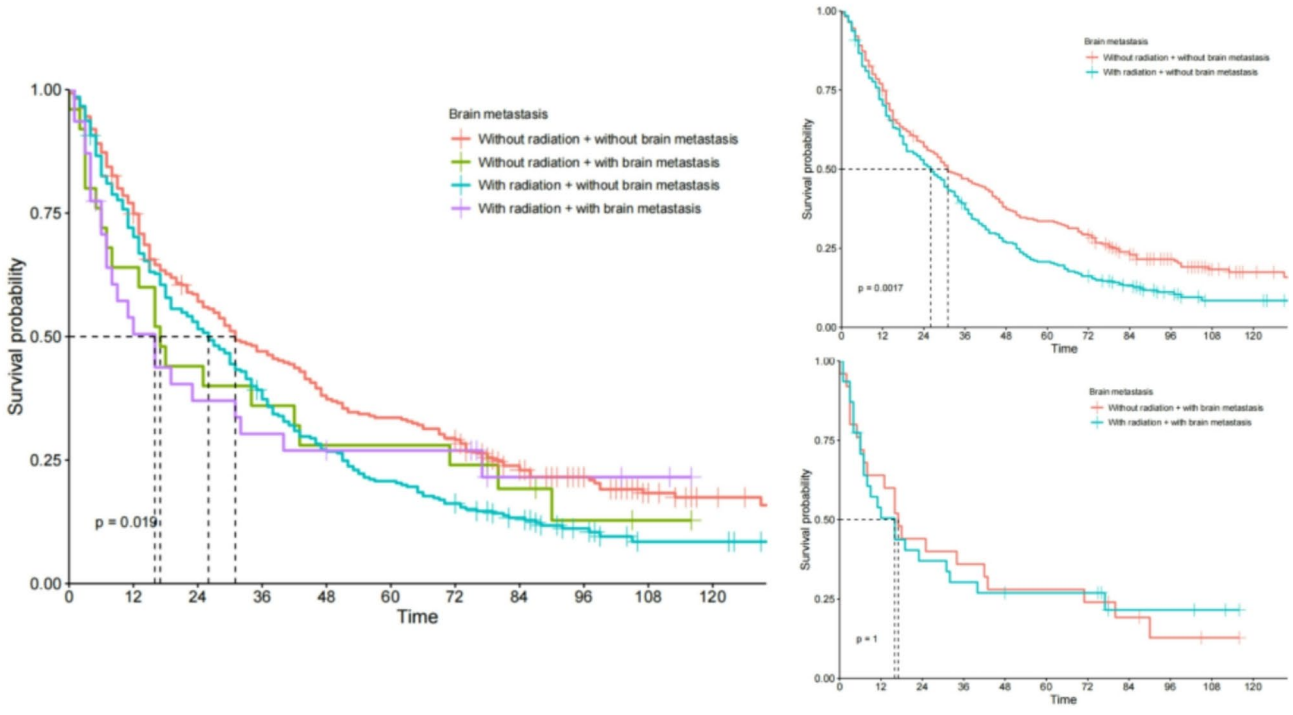

Fig. 4. Survival curve of surgically treated mccRCC patients by radiotherapy and brain metastasis.

the impact of radiotherapy on the prognosis of surgically treated mccRCC and identify independent factors that may affect patient survival. We employed propensity score matching (PSM) to minimize selection bias and potential confounding factors.

Our findings indicate that radiotherapy significantly reduces overall survival in patients with mccRCC who have undergone cytoreductive surgery. Subgroup analysis revealed that the efficacy of radiotherapy is

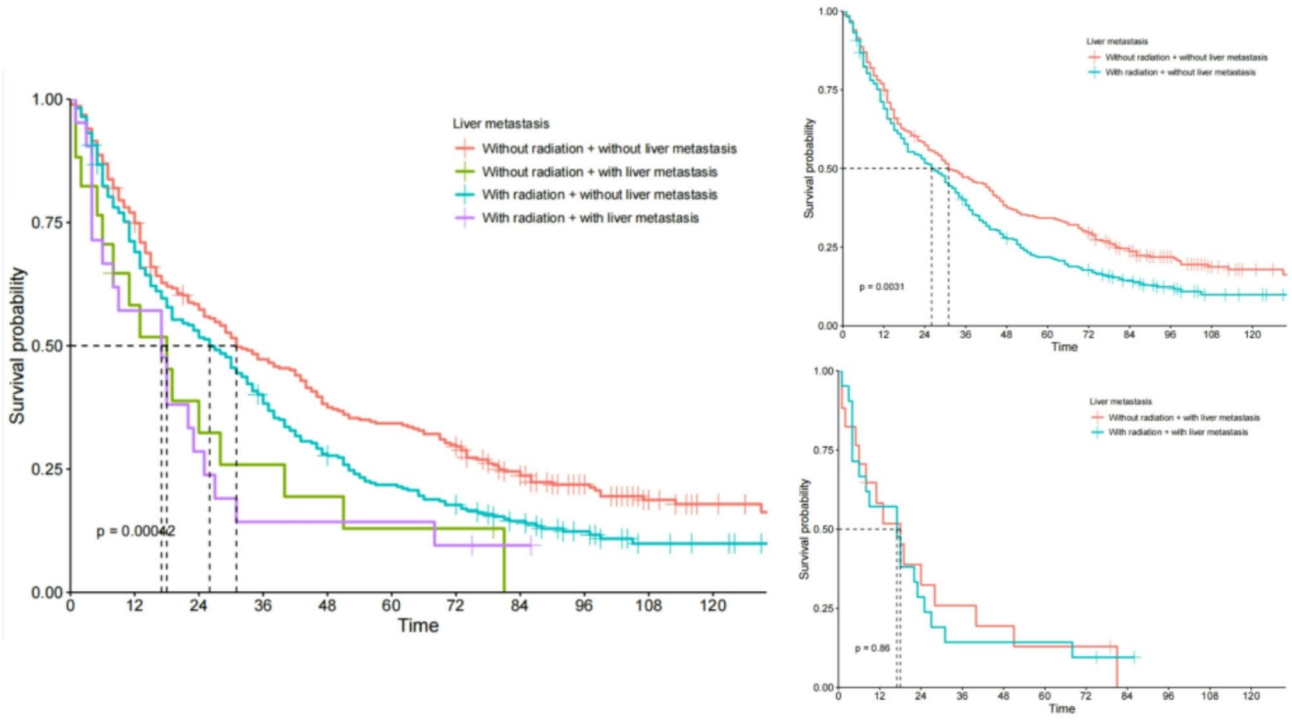

Fig. 5. Survival curve of surgically treated mccRCC patients by radiotherapy and liver metastasis.

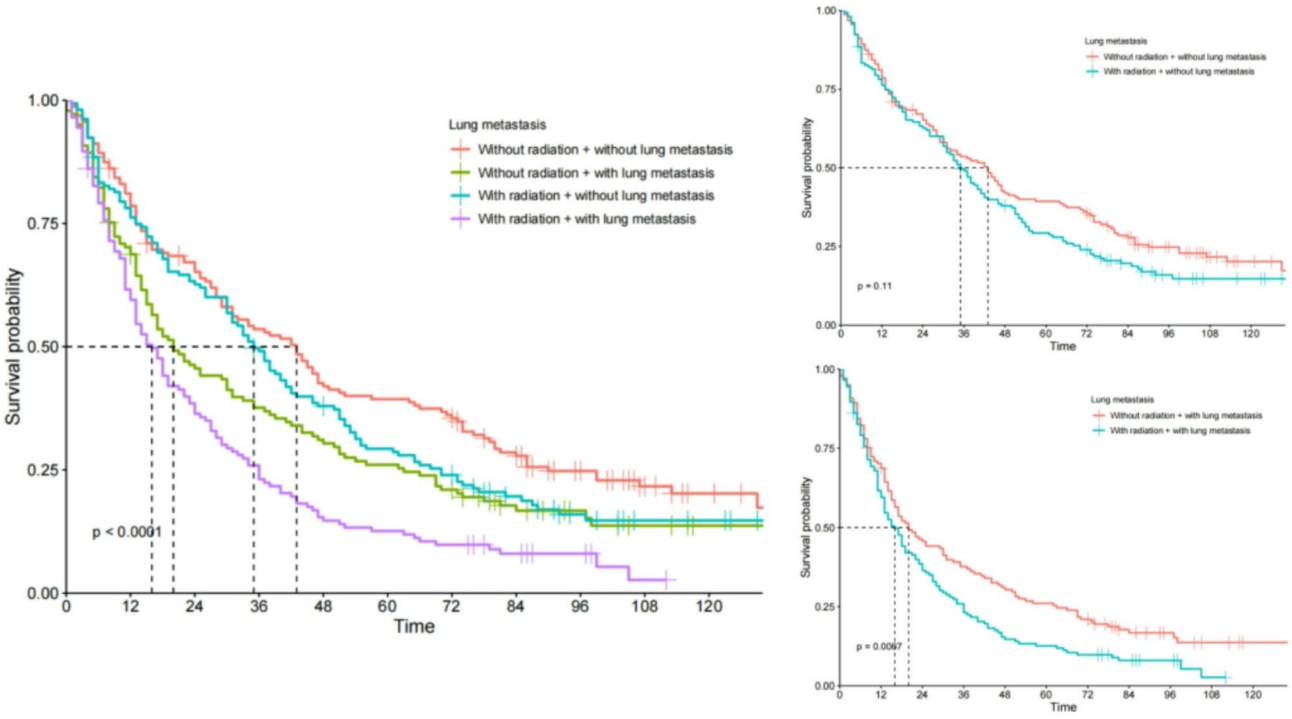

Fig. 6. Survival curve of surgically treated mccRCC patients by radiotherapy and lung metastasis.

Variable	Univariate analysis			Multivariate analysis		
	HR	(95% CI)	*P*	HR	(95% CI)	*P*
Age						
< 60	1.00					
≥ 60	0.98	(0.82, 1.17)	0.808			
Sex						
Male	1.00					
Female	1.02	(0.84, 1.24)	0.861			
Race						
White	1.00					
Black	1.03	(0.66, 1.59)	0.899			
Other	0.95	(0.65, 1.37)	0.767			
Marital status						
Married	1.00					
Single/Unknown	0.97	(0.81, 1.17)	0.769			
Size						
< 7 cm	1.00			1.00		
≥ 7 cm	1.20	(1.00, 1.44)	0.050	0.90	(0.70, 1.15)	0.389
Grade						
Grade I/II	1.00			1.00		
Grade III	1.79	(1.37, 2.33)	< 0.001	1.50	(1.13, 2.00)	< 0.001
Grade IV	2.72	(2.06, 3.58)	< 0.001	1.95	(1.43, 2.67)	< 0.001
Unknown	1.36	(0.98, 1.90)	0.068	1.16	(0.82, 1.63)	0.408
T						
T1	1.00			1.00		
T2	0.97	(0.70, 1.35)	0.874	1.02	(0.68, 1.53)	0.928
T3	1.73	(1.37, 2.18)	< 0.001	1.26	(0.93, 1.71)	0.131
T4	1.78	(1.19, 2.67)	< 0.001	1.09	(0.68, 1.74)	0.731
N						
N0	1.00			1.00		
N1	1.91	(1.53, 2.36)	< 0.001	1.53	(1.22, 1.92)	< 0.001
Radiation						
No/Unknown	1.00			1.00		
Yes	1.31	(1.10, 1.56)	0.003	1.30	(1.08, 1.55)	< 0.001
Chemotherapy						
No/Unknown	1.00			1.00		
Yes	1.34	(1.12, 1.60)	0.002	1.07	(0.89, 1.30)	0.479
Lung metastasis						
No/Unknown	1.00			1.00		
Yes	1.57	(1.32, 1.87)	< 0.001	1.28	(1.08, 1.55)	0.013
Liver metastasis						
No/Unknown	1.00			1.00		
Yes	1.73	(1.22, 2.46)	0.002	1.48	(1.03, 2.14)	0.035
Bone metastasis						
No/Unknown	1.00					
Yes	1.06	(0.88, 1.29)	0.530			
Brain metastasis						
No/Unknown	1.00					
Yes	1.34	(0.43, 1.55)	0.414			

Table 2. Univariate and multivariate analyses for MccRCC.

particularly detrimental to survival in patients without brain, bone, or liver metastases, as well as in those with lung metastases. Additionally, Cox regression analysis identified tumor grade, lymph node metastasis, lung metastasis, and liver metastasis as independent factors influencing patient prognosis, beyond the effects of radiotherapy. We incorporated these indicators into a nomogram to explore their impact on one-year, three-year, and five-year survival rates for patients with mccRCC undergoing cytoreductive surgery (Fig. 7).

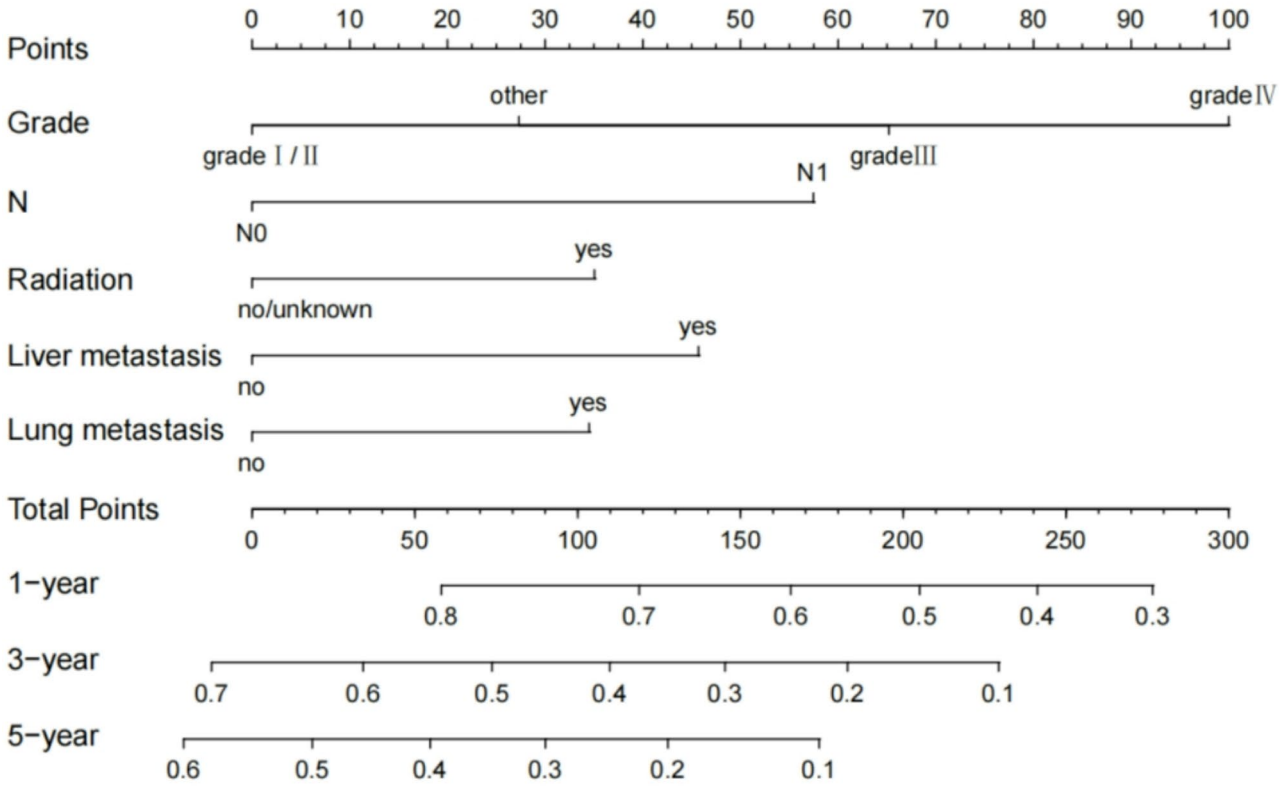

Fig. 7. Nomogram construction of surgically treated mccRCC patients by multivariate cox regression analysis.

The reasons for the disadvantage of postoperative radiotherapy in patients with mccRCC may come from the following aspects. Firstly, radiotherapy not only targets tumor cells but may also affect the surrounding tissues and organs[15,16], thus triggering some radiotherapy-related complications, such as radiation enteritis[17]. Once these complications occur, they will deteriorate the patient's physical condition after surgery and ultimately affect the patient's survival. In addition, postoperative radiotherapy may suppress the immune system. The immune system plays a crucial role in fighting cancer. Radiation can damage immune cells and affect the body's immune response[18]. A weakened immune system may reduce its ability to recognize and eliminate residual cancer cells, thereby increasing the risk of cancer recurrence and metastasis[19,20]. Moreover, radiotherapy may trigger genetic and molecular changes in cancer cells. Although the aim of radiotherapy is to kill cancer cells, it may also cause some cancer cells to undergo genetic mutations or epigenetic changes. These changes will make cancer cells more resistant to treatment or more invasive, thus worsening the patient's prognosis[21]. Furthermore, early research by Lei Yao and others has found that ccRCC, a specific type of tumor, is not sensitive to radiotherapy and chemotherapy[22–24]. Therefore, in the treatment of mccRCC, radiotherapy has been placed in a position after targeted therapy and immunotherapy. Notably, Siva S and colleagues discovered that the combination of radiotherapy and immunotherapy can be beneficial for patient prognosis, and this effect is influenced by the radiation dose, possibly due to high-dose radiation stimulating anti-tumor immune capabilities[25,26]. Nevertheless, in clinical practice, it is essential to conduct individualized analysis based on the patient's specific condition to facilitate the formulation of treatment strategies. Although this study has demonstrated that the significant efficacy of radiotherapy is detrimental to the survival of mccRCC patients undergoing cytoreductive surgery, it still has certain limitations. Firstly, as a retrospective study, despite the use of the PSM method, it is still not possible to completely eliminate all biases. Secondly, detailed records of radiotherapy information, such as specific radiotherapy targets and radiotherapy doses, are not available in the SEER database. These factors may affect the prognosis of patients. Furthermore, targeted therapy and immunotherapy have been proven to play important roles in clear cell renal carcinoma and have been clinically applied. However, the SEER database lacks information on targeted therapy and immunotherapy. Therefore, further validation of this study is needed through multi-center, randomized controlled clinical trials.

Conclusions

mccRCC is a challenging disease that requires multidisciplinary management and multimodal therapy. Although cytoreductive surgery can improve patients' quality of life, postoperative radiotherapy may adversely affect the prognosis of mccRCC patients, reducing their median survival by approximately 6 months.

Data availability

The datasets for this study can be found in the SEER*Stat Software (cancer.gov). The original contributions presented in the study are included in the article.

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8. References

1. Xu, L. et al. *Deep learning using CT images to grade clear cell renal cell carcinoma: development and validation of a prediction model. Cancers (Basel)* **14**(11). (2022).
2. Bukavina, L. et al. Epidemiology of renal cell carcinoma: 2022 update. *Eur. Urol.* **82** (5), 529–542 (2022).
3. Brozovich, A. et al. All bone metastases are not created equal: revisiting treatment resistance in renal cell carcinoma. *J. Bone Oncol.* **31**, 100399 (2021).
4. Young, M. et al. Renal cell carcinoma. *Lancet* **404**(10451): 476–491. (2024).
5. Yang, W. et al. Machine learning to improve prognosis prediction of metastatic clear-cell renal cell carcinoma treated with cytoreductive nephrectomy and systemic therapy. *Biomol. Biomed.* **23** (3), 471–482 (2023).
6. Hsieh, P. Y. et al. The effect of metastasectomy on overall survival in metastatic renal cell carcinoma: A systematic review and meta-analysis. *Urol. Oncol.* **39** (7), 422–430 (2021).
7. Nolazco, J. I. & Chang, S. L. Role of surgery in metastatic renal cell carcinoma. *Hematol. Oncol. Clin. North. Am.* **37** (5), 893–905 (2023).
8. Jiang, W. et al. Impact of primary tumor size on prognosis in patients with metastatic renal cell carcinoma receiving cytoreductive nephrectomy: A population study of a Chinese center and the US SEER database. *Technol. Cancer Res. Treat.* **20**, 15330338211019507 (2021).
9. Ali, M. et al. The role of stereotactic ablative body radiotherapy in renal cell carcinoma. *Eur. Urol.* **82** (6), 613–622 (2022).
10. Marvaso, G. et al. Oligo metastatic renal cell carcinoma: stereotactic body radiation therapy, if, when and how? *Clin. Transl Oncol.* **23** (8), 1717–1726 (2021).
11. Wang, B., Xue, Y. & Zhai, W. Integration of tumor microenvironment in Patient-Derived organoid models help define precision medicine of renal cell carcinoma. *Front. Immunol.* **13**, 902060 (2022).
12. An, W. et al. Analysis of related risk factors and prognostic factors of gastric Cancer with liver metastasis: A SEER and external validation based study. *Int. J. Gen. Med.* **16**, 5969–5978 (2023).
13. Wei, Q. et al. The promising role of radiotherapy in the treatment of advanced or metastatic renal cell carcinoma: a narrative review. *Transl Androl. Urol.* **9** (6), 2821–2830 (2020).
14. Huang, L. et al. The LncRNA signatures of genome instability to predict survival in patients with renal Cancer. *J. Healthc. Eng.* **2021**, 1090698 (2021).
15. Thirupathi, K. et al. Thermosensitive Polymer-Modified mesoporous silica for pH and Temperature-Responsive drug delivery. *Pharmaceutics* **15**(3). (2023).
16. Pan, X. et al. Gold Nanocage-Based multifunctional nanosensitizers for programmed photothermal /Radiation/Chemical coordinated therapy guided by FL/MR/PA multimodal imaging. *Int. J. Nanomed.* **18**, 7237–7255 (2023).
17. Moraitis, I. et al. Mucosal macrophages govern intestinal regeneration in response to injury. *Gastroenterology* (2025).
18. Ma, Z. et al. Respiratory adverse effects in patients treated with immune checkpoint inhibitors in combination with radiotherapy: a systematic review and meta-analysis. *Radiat. Oncol.* **19** (1), 134 (2024).
19. Zhang, W., Wu, M. & Huang, Y. Engineered CARD11-PIK3R3 T-cell therapies as weapons of cancer mass destruction. MedComm (2020). 5(7), e628. (2024).
20. Jin, G. et al. Polymeric immunogel prevents tumor recurrence and metastasis by dual activation of innate and adaptive immunity. *Bioact Mater.* **45**, 102–114 (2025).
21. Xu, X. et al. Metabolic reprogramming and epigenetic modifications in cancer: from the impacts and mechanisms to the treatment potential. *Exp. Mol. Med.* **55** (7), 1357–1370 (2023).
22. Yao, L. et al. GSDMs are potential therapeutic targets and prognostic biomarkers in clear cell renal cell carcinoma. *Aging (Albany NY).* **14** (6), 2758–2774 (2022).
23. Chen, G. et al. A model to predict prognosis of renal cell clear cell carcinoma based on 3 Angiogenesis-related long Non-coding RNAs. *J. Cancer.* **15** (11), 3481–3494 (2024).
24. Qin, J. et al. Long Non-Coding RNA PCED1B-AS1 promotes the progression of clear cell renal cell carcinoma through miR-484/ZEB1 Axis. *Onco Targets Ther.* **14**, 393–402 (2021).
25. Zalay, O. et al. Adjuvant radiotherapy for upper tract urothelial carcinoma: systematic review and Meta-Analysis. *Curr. Oncol.* **30** (1), 19–36 (2022).
26. Siva, S. et al. Radiotherapy for renal cell carcinoma: renaissance of an overlooked approach. *Nat. Rev. Urol.* **14** (9), 549–563 (2017).

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Declarations

Competing interests

The authors declare no competing interests.

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