Review Article

# Survival rate comparisons of angioembolization and neoadjuvant targeted therapy on unresectable renal cell carcinoma patients: A systematic review

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## Abstract

**Objective:** Renal cell cancer (RCC) is the most typical form of kidney cancer in adults, which accounts for 80% to 85% of all primary renal neoplasms. RCC develops inside the renal cortex. This study aimed to systematically review the survival rate of patients treated with targeted therapy and/or RC. Surgery is the standard therapy for RCC, even though after surgery, 20%–40% of patients with localized RCC would experience distant metastases. Metastases or large RCC are not amenable to surgery. Unresectable RCC can be treated palliatively with angioembolization or neoadjuvant therapy. This study aims to review the survival rate comparisons of angioembolization and neoadjuvant targeted therapy on unresectable renal cell carcinoma.

**Methods:** A thorough search across databases such as PubMed, Cochrane Library, and ProQuest was conducted for articles published from 2018 to 2023. To uphold research integrity, duplicates, reviews, and incomplete articles were excluded, ensuring only pertinent and original research findings for subsequent analysis.

**Results:** Database search yielded 247 articles, which were systematically eliminated, leaving 6 relevant articles. Analyzed articles showed the overall survival of patients treated with angioembolization and neoadjuvant agents.

**Conclusion:** Unresectable RCC can be treated palliatively with angioembolization. Angioembolization may improve clinical effectiveness and lessen side effects by boosting local concentrations of drugs. Drug-eluting bead transarterial chemoembolization is a novel embolization option that can embolize the arteries that feed the tumor and cutoff the blood supply to the tumor. Sunitinib, the most studied medicinal agent, was found to have higher effectiveness when combined with angioembolization.

**Keywords:** Angioembolization, RCC, survival rate, targeted therapy

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## INTRODUCTION

Renal cell carcinoma (RCC) distinguishes itself as the predominant variant of kidney cancer in the adult demographic, comprising a noteworthy 80%–85% of all primary renal neoplasms and specifically manifesting its deleterious effects within the intricate confines of the

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renal cortex. The intricate development of RCC unfolds under the multifaceted influence of a myriad of uncertain factors, encompassing genetic predispositions, smoking habits, the inevitability of aging, obesity, hormonal fluctuations, hypertension, chronic renal failure, dietary proclivities, and occupational exposures. Notably, amid the diverse pathological subtypes characterizing renal cell carcinoma, clear cell renal cell carcinoma asserts its prominence, constituting a significant majority at 80%, followed by papillary renal cell carcinoma (10%–15%) and chromophobe cell carcinoma (5%).[1-4] This malignant landscape presents a sobering 5-year death rate, soaring to 16.9%, underscoring RCC's exceptionally high lethality. The gravity of this grim statistic is attributable, in part, to a substantial cohort of patients grappling with localized Stage III and/or advanced Stage IV disease, thereby exerting a profound impact on the overall mortality landscape. Moreover, the persistent elevation in mortality rates is further complicated by the relatively heightened incidence of disease recurrence and metastases postsurgical resection, particularly evident in patients contending with high-risk localized disease. This intricate clinical scenario accentuates the multifaceted and challenging nature inherent in the management of RCC.[3,5]

During its initial stages, renal cell carcinoma (RCC) frequently unfolds without evident symptoms, and the discovery of a solid renal mass commonly takes place serendipitously through routine radiological examinations. A meager 10% of individuals exhibit the classical clinical triad marked by flank discomfort, hematuria, and the presence of a palpable flank tumor. This subtle clinical presentation underscores the challenging nature of early detection, as the majority of cases remain asymptomatic until the disease has progressed further. The fortuitous identification of a solid renal mass during routine radiological assessments highlights the importance of vigilant screening and diagnostic measures in uncovering RCC in its incipient stages.[6,7] The primary therapeutic approach for early-stage RCC devoid of metastases remains the surgical excision of the primary tumor. Nonetheless, a considerable proportion of RCC patients, approximately 30%, already harbor distant metastases at the time of initial diagnosis. Postsurgical intervention, a noteworthy 20%–40% of patients with localized RCC may subsequently encounter the development of distant metastases, emphasizing the nuanced challenges in managing RCC and its propensity for advanced disease even after seemingly successful surgical intervention.[8,9]

Over the past several decades, there have been numerous breakthroughs in the management of advanced RCC. Unresectable RCC can be treated palliatively with transarterial chemoembolization (TACE). This procedure can improve clinical effectiveness and lessen side effects compared to systemic chemotherapy by boosting local drug concentration.[10-12] Traditional TACE often employed emulsions of chemotherapeutic medicines and lipiodol; however, medications cannot be released slowly enough or have a long enough residence period. In addition to this, neoadjuvant treatment has the potential to reduce the size of advanced tumors, making surgical operations possible in cases where they would not have been safe or practical due to unresectable locoregional illness.[13] Therefore, we planned to systematically review the survival rate comparisons of angioembolization and neoadjuvant chemotherapy on unresectable renal cell carcinoma.

## METHODS

Conducted as a systematic review, this study employed a rigorous approach by systematically searching the literature across diverse databases. The systematic literature search spanned key repositories, including PubMed, Google Scholar, the Directory of Open Access Journals, and Cochrane Database of Systematic Reviews. This comprehensive search strategy was meticulously designed to ensure a thorough and inclusive examination of existing scholarly works, encompassing a range of authoritative platforms. By leveraging these reputable databases, the study aimed to gather a comprehensive and diverse array of relevant articles, thereby enriching the depth and breadth of the systematic review process. The search was conducted in English, using keywords related to the survival rate of targeted therapy and angioembolization on renal cell carcinoma patients, with the keywords used were "survival rate" OR "morbidity rate" AND "angioembolization" OR "chemoembolization" AND "neoadjuvant" AND "chemotherapy" AND "renal cell carcinoma" OR "RCC" OR "unresectable renal cell carcinoma" OR "unresectable RCC." The search methodology employed in this investigation entailed the utilization of a strategic combination of specific keywords, selectively applied to both the title and abstract sections of the articles under consideration. This targeted approach sought to refine the search process and enhance the precision of identifying pertinent literature. The inclusion of keywords served as a deliberate criterion for filtering and selecting articles that align with the study's objectives. It is noteworthy that this search endeavor was delimited to publications within the specific timeframe spanning from 2018 to 2023, ensuring the retrieval of the most recent and relevant contributions to the field. This temporally constrained focus enhances the study's currency and relevance, aligning the gathered

information with contemporary developments in the subject matter.

This study encompassed a diverse range of study designs to comprehensively address the research objectives. The scope of the investigation extended to interventions in both adult and pediatric patients, provided there was complete and relevant data on pediatric subjects. The data extraction process was meticulously executed through the utilization of a standardized table, incorporating essential details such as author names, publication year, study design, study setting, participant numbers, treatment modalities employed, and key findings from each study. Following the initial search and filtration based on predefined keywords, a manual analysis of articles was conducted, evaluating the relevance of titles and abstracts. Articles meeting the predefined inclusion and exclusion criteria, with any ambiguity, underwent further scrutiny through a comprehensive examination of the full text. The extracted information from these articles was systematically recorded in the data extraction table.

In the subsequent phase of the research process, a comprehensive and meticulous comparative analysis was conducted to examine and juxtapose the obtained results from the studies included in the investigation. This analytical approach extended beyond the confines of the current study, encompassing a thorough examination of findings documented in other systematic reviews and pertinent literature within the field. By engaging in this comparative exploration, the research aimed to foster a more nuanced and comprehensive understanding of the broader landscape within the relevant research domain. This methodological endeavor not only added depth to the interpretation of the gathered data but also facilitated the identification of potential patterns, trends, and divergences that contribute to advancing the scholarly discourse in a more informed and contextualized manner.

## RESULTS

### Study selection

A systematic search was carried out and yielded 247 articles [Figure 1]. Culminating in the identification of 247 articles, as illustrated in Figure 1. Subsequent scrutiny and exclusion of duplicate entries resulted in a refined pool of 98 articles. Following a stringent eligibility assessment, 31 articles emerged as fitting the criteria for inclusion in this study. A detailed examination of the full-text content further refined the selection, ultimately incorporating an additional 6 articles. The outcomes of the database search are systematically delineated in Table 1 and visually represented in Figure 1.

### Included articles

Out of the six studies incorporated in the analysis, three adopted a randomized controlled study design, ensuring a rigorous and unbiased approach to data collection and analysis. In addition, one study employed a nonrandomized controlled design, enhancing the breadth of methodological diversity. Furthermore, two studies were characterized as retrospective cohort studies, providing valuable insights into the outcomes and variables of interest over time. This diverse array of study designs contributes to a comprehensive understanding of the subject matter, encompassing both controlled and observational methodologies to enrich the overall robustness of the findings

### Populations

A total of 1230 patients were involved in the eight included studies. Almost all studies were single-center randomized controlled studies.

## DISCUSSION

RCC is a cancerous tumor that develops from the tubular epithelium and accounts for 80%–90% of renal malignancies.[1,19] This carcinoma is the 17$^{th}$ most prevalent cancer in the world, accounting for 2.2% of all cancer diagnoses in 2018. RCC had an estimated 403.262 new cases of diagnosis worldwide in 2018, and there were also 175.098 fatalities.[20] Uncertain factors, including genetics, smoking, obesity, hormone levels, hypertension, food, and work environment, may contribute to RCC.[2,3]

Considering that the 5-year death rate was 16.9%, the risk of RCC recurrence is quite high. The most successful treatment for early RCC without metastases is still surgical excision of the main tumor. For the majority of localized and locally progressed RCC, extirpative surgery, by radical or partial nephrectomy, continues to be the cornerstone of final therapy. However, patients who have metastatic disease upon presentation often have a bad prognosis, with a 2-year survival rate of only 18%. Radical nephrectomy decreases mortality in localized disease and can result in long-term disease-free life. However, about 30% of RCC patients already have distant metastases when they are first diagnosed. After surgery, 20%–40% of patients with localized RCC would experience distant metastases.[21-23]

RCC exhibits a complex and diverse biological behavior, with one of its distinctive characteristics being the propensity for invasion into the venous system. The incidence of venous tumor thrombus in RCC ranges from 5% to 15%, and renal venous tumor thrombus stands out as the most prevalent, accounting for 60%–78% of

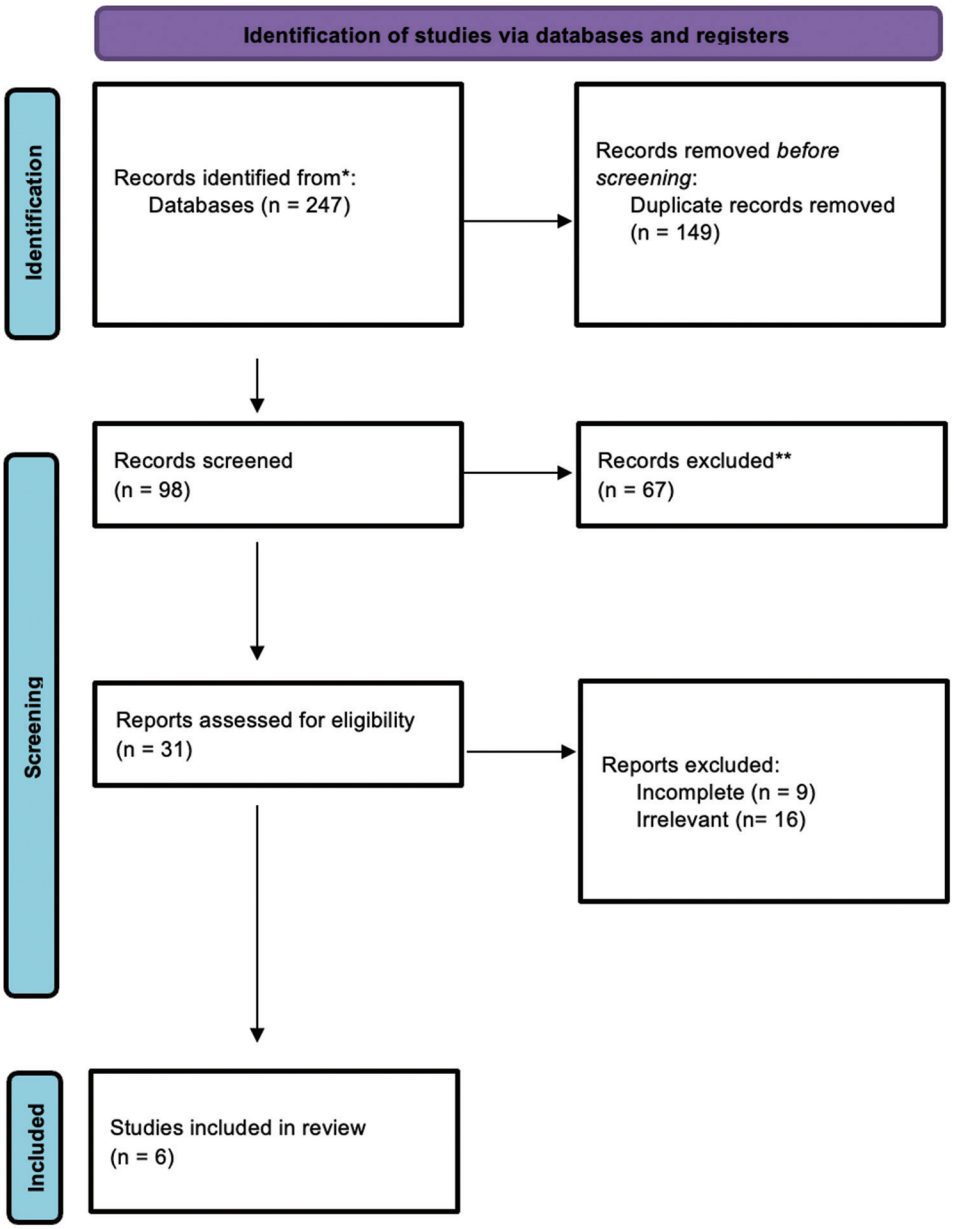


**Figure 1:** Systematic search

all venous tumor thrombi. A tumor thrombus within the renal vein may extend into the vein itself or potentially reach the right atrium. In addressing advanced renal cell carcinoma, conventional chemoradiotherapy often proves ineffective, leading to the predominant use of molecular-targeted medications and immunotherapy. Notably, three frequently utilized multitargeted tyrosine kinase inhibitors (TKIs) – sunitinib, sorafenib, and pazopanib – play a pivotal role in the molecularly targeted treatment landscape for RCC. However, a significant challenge arises as these targeted medications commonly encounter drug resistance and disease progression over time, impacting the overall survival (OS) outcomes for patients grappling with advanced RCC.[24-27]

## Neoadjuvant therapy

Categorized based on their mechanisms of action, targeted medications for renal cell carcinoma (RCC) can be broadly classified into three distinct categories. In the intricate landscape of cancer therapeutics, the focal point is occupied by upstream inhibitors, strategically designed to obstruct the mTOR pathway entrenched within tumors. This deliberate interference seeks to disrupt the molecular intricacies orchestrating tumorigenic processes upstream. Simultaneously, the role of intermediate monoclonal antibodies emerges as pivotal, zeroing in on the neutralization of vascular endothelial growth factor-A (VEGF-A) secreted by tumor cells. This targeted approach aims to counteract the proangiogenic signals

**Table 1: Study characteristics and finding**

| Author | Design | Country | Subjects | Age (year) | Agent | Findings |
|---|---|---|---|---|---|---|
| Lu *et al*., 2023[14] | Retrospective cohort | China | 98 | TACE + sunitinib: 58.5±9.1<br>Sunitinib: 55.8±12.9 | TACE + sunitinib versus sunitinib | The intervention involving TACE combined with sunitinib in this study demonstrated an exceptionally high technical success rate of 100%, underscoring the efficacy of this approach. Remarkably, the TACE + sunitinib group exhibited superior outcomes across a spectrum of parameters when compared to the group receiving sunitinib alone. Notably, the TACE + sunitinib cohort displayed a significantly elevated ORR of 66.0%, surpassing the ORR of 39.2% observed in the sunitinib-only group. Furthermore, the TACE + sunitinib group demonstrated an impressive DCR of 85.1%, contrasting with the 66.7% DCR recorded in the sunitinib-only group. The clinical advantages of adopting the TACE + sunitinib approach extended to prolonged OS and PFS. Specifically, the mPFS in the TACE + sunitinib group reached 15.6 months, outperforming the sunitinib-only group's mPFS of 10.9 months. Moreover, the TACE + sunitinib group exhibited a longer mOS at 35.0 months, compared to the sunitinib group's mOS of 25.7 months. These compelling findings underscore the potential synergistic benefits of combining TACE with sunitinib, suggesting not only improved technical efficacy but also superior clinical outcomes in the comprehensive management of the studied population. This robust evidence points towards the promising prospects of the TACE + sunitinib intervention as a valuable therapeutic strategy in the context of the specific population under investigation |
| Bi *et al*., 2022[13] | Retrospective cohort | China | 35 | 67.5±10.8 | DEB-TACE with doxorubicin | At the posttreatment intervals of 1, 3, and 6 months subsequent to DEB-TACE, the observed ORR and DCR were noteworthy, standing at 47.1% and 94.1%, 29.0% and 87.1%, 23.1% and 84.6%, respectively. The PFS exhibited favorable rates of 84.7%, 73.7%, and 62.3% at 3, 6, and 12 months, culminating in a median PFS of 21.4 months. Similarly, the OS rates at 3, 6, and 12 months were commendable, recording percentages of 93.9%, 87.6%, and 65.2%, respectively, with a median OS of 24.6 months. Importantly, the safety profile of DEB-TACE was robust, with no recorded treatment-related fatalities or serious adverse events rated at grade 3 or higher throughout the study duration. These findings underscore the efficacy and safety of DEB-TACE as a therapeutic modality for the studied population, with sustained positive outcomes in both response rates and survival metrics |
| Gross-Goupil *et al*., 2018[15] | Randomized control trial | USA | 724 | ≤18 years and ≥65 years | Axitinib | In the assessment conducted at posttreatment intervals of 1, 3, and 6 months following the administration of DEB-TACE, the obtained ORR and DCR showcased notable efficacy, registering at 47.1% and 94.1%, 29.0% and 87.1%, and 23.1% and 84.6%, respectively. The PFS demonstrated consistently favorable rates, reaching 84.7%, 73.7%, and 62.3% at 3, 6, and 12 months, cumulatively resulting in a median PFS of 21.4 months. Similarly, the OS rates at 3, 6, and 12 months were commendable, reflecting percentages of 93.9%, 87.6%, and 65.2%, respectively, with a median OS of 24.6 months. Crucially, the safety profile of DEB-TACE exhibited robustness, as evidenced by the absence of recorded treatment-related fatalities or serious adverse events rated at grade 3 or higher throughout the duration of the study. These compelling findings not only underscore the demonstrated efficacy but also the safety of DEB-TACE as a therapeutic modality for the studied population, showcasing sustained positive outcomes in both response rates and survival metrics. This comprehensive evaluation reinforces the potential of DEB-TACE as a viable and well-tolerated treatment approach, thereby contributing to the expanding landscape of therapeutic options for the specific population under investigation |

*Contd...*

**Table 1: Contd...**

| Author | Design | Country | Subjects | Age (year) | Agent | Findings |
|---|---|---|---|---|---|---|
| Lebacle *et al*., 2019[16] | Nonrandomized trial | France | 18 | 60.4±9.7 | Axitinib | Within the cohort of 18 subjects, an overwhelming majority of 16 individuals demonstrated a discernible reduction in tumor diameter subsequent to the implementation of neoadjuvant therapy involving axitinib. The calculated median size reduction was quantified at a noteworthy 17%, with the median tumor size exhibiting a decrease from the initial measurement of 76.5 mm to a posttreatment dimension of 64.0 mm. It is particularly noteworthy that 12 patients who underwent PN for tumors initially measuring less than 7 cm were deemed to have successfully achieved the primary objective of the study. However, it is imperative to acknowledge the nuanced nature of therapeutic responses, as evidenced by the fact that over the 2-year follow-up period, six patients encountered metastatic progression, and an additional two experienced recurrence. This highlights the intricacies of the therapeutic journey and emphasizes the ongoing need for vigilance in the comprehensive assessment of long-term outcomes. These compelling findings not only shed light on the potential efficacy of axitinib neoadjuvant therapy in instigating substantial tumor size reduction, particularly in the context of PN for smaller tumors but also underscore the imperative nature of vigilant monitoring for metastatic progression and recurrence over an extended follow-up duration, enriching our understanding of the dynamic interplay between therapeutic interventions and disease progression |
| Motzer *et al*., 2019[17] | Randomized control trial | USA | 886 | Avelumab plus axitinib: 62 (29–83) Sunitinib: 61 (27–88) | Avelumab, axitinib, sunitinib | Patients undergoing first-line therapy for advanced renal-cell carcinoma, through the innovative combination of avelumab and axitinib or traditional sunitinib, experienced a remarkable extension in progression-free survival, surpassing the outcomes associated with conventional treatments. The median progression-free survival demonstrated a noteworthy increase, escalating from 8.4 months to an impressive 13.8 months with the utilization of avelumab and axitinib. Particularly remarkable was the substantial enhancement in the objective response rate among patients harboring PD-L1-positive tumors who received avelumab in conjunction with axitinib, reaching an outstanding 55.2%, in stark contrast to the 25.5% observed with the administration of sunitinib alone. These compelling findings, elucidated over a median follow-up for overall survival spanning 11.6 months for avelumab with axitinib and 10.7 months for sunitinib, underscore the considerable efficacy and potential advantages associated with this innovative combination therapy. The outcomes are particularly notable in the subset of patients with PD-L1-positive tumors, emphasizing the potential for enhanced therapeutic responses and prolonged disease control in this specific and clinically significant population. This paradigm-shifting approach holds promise in reshaping the landscape of treatment strategies for advanced renal-cell carcinoma, offering improved outcomes and a more targeted therapeutic response |
| Rini *et al*., 2019[18] | Randomized control trial | USA | 861 | Pembrolizumab-axitinib: 62 (30–89) Sunitinib: 61 (26–90) | Pembrolizumab, axitinib, sunitinib | Following a median follow-up duration of 12.8 months, the cohort subjected to treatment with the pembrolizumab-axitinib combination demonstrated a striking advantage in overall survival. The estimated proportion of patients still alive at the 12-month milestone reached an impressive 89.9%, significantly exceeding the 78.3% observed in the group receiving |

*Contd...*

**Table 1: Contd...**

| Author | Design | Country | Subjects | Age (year) | Agent | Findings |
|---|---|---|---|---|---|---|
| | | | | | | sunitinib. This significant distinction was further accentuated by the calculation of a hazard ratio for death, which stood at 0.53. This numerical value denotes a noteworthy and substantial reduction in the risk of mortality associated with the treatment regimen involving pembrolizumab-axitinib. This statistical insight not only emphasizes the effectiveness of the mentioned therapeutic approach but also underscores its potential in enhancing patient outcomes. Moreover, the comparison of median progression-free survival between the pembrolizumab-axitinib group and the sunitinib group revealed a noteworthy disparity. The former exhibited a prolonged median progression-free survival of 15.1 months, surpassing the 11.1 months observed in the latter. This extended duration of progression-free survival in the pembrolizumab-axitinib group signifies a promising aspect of the treatment's efficacy, providing clinicians and researchers with valuable data to consider in the ongoing exploration of optimal therapeutic strategies for improved patient care in this medical context. These compelling findings not only underscore a significant survival benefit linked to the pembrolizumab-axitinib combination but also emphasize its efficacy in contributing to a prolonged progression-free interval. Collectively, these outcomes position the pembrolizumab-axitinib combination as a promising and potentially transformative therapeutic option for individuals contending with advanced renal-cell carcinoma, showcasing its potential to redefine treatment standards and improve outcomes in this challenging clinical context |

TACE: Transarterial chemoembolization, DCR: Disease control rate, ORR: Objective response rate, PFS: Progression-free survival, OS: Overall survival, mPFS: Median PFS, mOS: Median OS, DEB-TACE: Drug-eluting bead transarterial chemoembolization, PN: Partial nephrectomy

emitted by tumors, curbing their capacity to induce the formation of new blood vessels. Venturing further downstream in the continuum of therapeutic strategies, TKIs come into play, honing in on receptors expressed specifically on vascular endothelial cells. This encompassing approach spans a spectrum of receptors, including VEGF receptors 1 and 2 (VEGFR1-2), platelet-derived growth factor receptor (PDGFR), stem cell growth factor receptor (c-KIT), and FMS-like tyrosine kinase 3 (FLT-3). Precision in targeting these receptors becomes paramount as downstream inhibitors strive to disrupt the intricate intracellular signaling pathways crucial for the survival and proliferation of vascular endothelial cells, contributing comprehensively to the suppression of tumor angiogenesis. This multifaceted and nuanced therapeutic strategy underscores the complexity inherent in contemporary approaches to cancer treatment, with each inhibitor tailored to address distinct molecular targets in the relentless pursuit of impeding tumorigenesis. Among these, sunitinib stands out as a prominent multitarget receptor TKI, effectively inhibiting major targets such as VEGFR1-2, PDGFR, c-KIT, and FLT-3. This comprehensive targeting strategy plays a pivotal role in impeding tumor angiogenesis and inhibiting the proliferation of tumor cells, collectively contributing to the prevention of tumor development and metastasis. Notably, sunitinib has emerged as a frequently utilized first-line medication in the treatment of RCC, reflecting its efficacy and established position in current therapeutic protocols for this malignancy. The nuanced and multifaceted approach of sunitinib in targeting key pathways underscores its significance as a cornerstone in the therapeutic landscape for RCC, solidifying its role as a pivotal player in the management of this complex malignancy.[25,28,29]

The reduction in primary tumor size stands out as a notable outcome in the application of TKIs for the treatment of metastatic RCC. Among these, sunitinib, administered over two cycles, has garnered extensive research attention and is considered a frontline therapeutic approach. A significant milestone in the therapeutic landscape occurred with the licensure of the oral inhibitor axitinib in 2012. Axitinib is specifically designed to target a range of receptors, exerting its therapeutic effects on VEGFR 1 through 3 (VEGFR1-3), c-KIT, and PDGFR. This targeted approach involves the inhibition of these critical receptors, disrupting the signaling pathways associated with VEGFs and PDGFRs. By selectively honing in on these molecular

targets, axitinib aims to impede the cascading cellular events that contribute to angiogenesis and tumor growth. This nuanced targeting of multiple receptors underscores the precision and specificity embedded in axitinib's mechanism of action, making it a valuable asset in the arsenal of targeted therapies against cancer. Axitinib offers a crucial therapeutic avenue, particularly after the inadequacy of previous systemic treatments. The exploration of diverse modalities continues to expand the array of therapeutic agents for RCC. Lebacle *et al*.'s study showcased the efficacy of axitinib neoadjuvant therapy, reporting a noteworthy median size reduction of 17%, especially significant in patients undergoing partial nephrectomy for tumors measuring <7 cm.[16] Motzer *et al*. delved into the first-line therapy realm with a study on avelumab with axitinib or sunitinib for advanced renal-cell carcinoma, revealing significantly prolonged progression-free survival (PFS), with a median PFS of 13.8 months compared to 8.4 months.[17] In addition, Rini *et al*.'s investigation highlighted improved OS rates in the pembrolizumab-axitinib group, with 89.9% of patients still alive at 12 months, presenting a notable hazard ratio for death of 0.53. The median PFS in the pembrolizumab-axitinib group was extended to 15.1 months, surpassing the 11.1 months observed in the sunitinib group. Axitinib's emphasis in this study stems from its potential efficacy, particularly in inhibiting vascular epidermal growth factor receptors compared to first-generation TKIs. A Phase III study comparing axitinib to sorafenib as second-line treatment for metastatic RCC demonstrated a significant objective response rate (ORR) of 19%, further solidifying its role as a promising and evolving therapeutic option in RCC management. This dynamic landscape showcases the continuous advancements in therapeutic strategies for metastatic RCC, with axitinib at the forefront of promising developments.[18]

### Transarterial chemoembolization

The palliative treatment of unresectable renal cell carcinoma (RCC) presents a viable option through TACE, offering potential improvements in clinical effectiveness and reduced side effects compared to systemic chemotherapy by enhancing local concentrations of drugs. Traditional TACE methodologies often involved the emulsion of chemotherapeutic agents with lipiodol. However, one limitation of this approach is the inadequate slow release of medications and a shorter residence period. This prompts the exploration of novel strategies and technologies within the realm of TACE, aiming to optimize drug delivery dynamics and prolong the therapeutic impact for individuals with unresectable RCC. The ongoing evolution of TACE techniques underscores the commitment to enhancing the efficacy and tolerability of palliative interventions, representing a crucial avenue in the comprehensive management of unresectable RCC.[10,30]

In the investigation conducted by Lu *et al*., the survival outcomes of unresectable patients were examined through the utilization of a combined treatment approach involving TACE and sunitinib. TACE emerges as an efficacious intervention for individuals grappling with advanced renal cell carcinoma (RCC) for whom surgical tumor removal is not a viable option. The TACE + sunitinib group demonstrated superior performance when compared to the group receiving sunitinib alone, particularly in terms of ORR and disease control rate. The integration of TACE with sunitinib showcased a notable extension in both PFS and OS for unresectable advanced RCC. Importantly, this combined therapy did not elevate the frequency of sunitinib-related adverse events, affirming its safety profile comparable to that of sunitinib alone. Consequently, the synergistic combination of TACE and sunitinib not only complements each other but also emerges as a secure and efficient therapeutic modality for the management of unresectable RCC. This study contributes valuable insights into the potential of combining these modalities to enhance treatment efficacy while maintaining a favorable safety profile in the challenging context of advanced RCC.[14]

The landscape of unresectable renal cell carcinoma (RCC) treatment has expanded with the introduction of a novel embolization option known as drug-eluting bead TACE (DEB-TACE). This innovative approach involves the embolization of arteries supplying the tumor, effectively cutting off its blood supply. What distinguishes DEB-TACE is its ability to gradually release anticancer medication locally, thereby extending the duration of tumor necrosis and enhancing therapeutic effectiveness. Unlike traditional interventions that may impact cavity organs such as the bladder and digestive system, DEB-TACE is primarily employed to treat unresectable cancers affecting significant organs. The study conducted by Bi *et al*. sheds light on the safety, practicality, and efficiency of DEB-TACE with doxorubicin-loaded CalliSpheres beads as a palliative therapy option for patients with unresectable RCC. This advancement represents a promising avenue in the comprehensive management of unresectable RCC, offering a targeted and effective approach that can contribute to improved patient outcomes and quality of life.[13]

A significant limitation observed in this literature evaluation pertains to the absence of research that directly compares the most recommended chemotherapy agents. To validate and enhance the robustness of our findings, there is a pressing need for a large-scale, multicenter, randomized,

and prospective study that specifically investigates the efficacy of different chemotherapy agents, providing valuable insights into the optimal treatment approaches. In addition, to comprehensively address the gaps in the current body of knowledge, further research in the form of meta-analysis is warranted. This approach can systematically synthesize existing data, potentially offering a more comprehensive and nuanced understanding of the diverse factors influencing treatment outcomes and patient responses. Such endeavors are pivotal for advancing the field and guiding evidence-based decision-making in the pursuit of optimal and personalized cancer treatment strategies.

## CONCLUSION

Over the past several decades, there has been a remarkable trajectory of breakthroughs in the management of advanced renal cell carcinoma (RCC), contributing to the expanding arsenal of therapeutic options. Palliative treatment for unresectable RCC has seen notable advancements through the application of TACE, offering potential enhancements in clinical effectiveness and a reduction in side effects compared to systemic chemotherapy. TACE achieves this by augmenting local concentrations of drugs, presenting a targeted approach to address the challenges posed by unresectable RCC. In addition, the emergence of DEB-TACE introduces a novel embolization option that not only embolizes arteries supplying the tumor but also disrupts the blood supply to the tumor, showcasing a promising avenue for intervention in these cases.

These therapeutic modalities, namely TACE and DEB-TACE, present safe and effective approaches in the palliative treatment of unresectable RCC, underscoring their significance in the evolving landscape of RCC management. Beyond embolization strategies, the utilization of TKIs has proven effective in reducing the size of the primary tumor in cases of metastatic RCC. Notably, sunitinib, a widely studied medicinal agent, has demonstrated heightened effectiveness when combined with TACE, revealing a potential synergistic interaction between these treatment modalities. This combination approach holds promise in optimizing treatment outcomes and represents a noteworthy avenue for further exploration in the realm of metastatic RCC management. Overall, these advancements collectively contribute to a more comprehensive and nuanced understanding of therapeutic strategies, paving the way for enhanced outcomes and improved quality of life for individuals grappling with advanced RCC.

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### Conflicts of interest

There are no conflicts of interest.

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