Beyond glomerular filtration rate: histological assessment of renal integrity after radiofrequency ablation for localized renal cell carcinoma

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Aim. To evaluate the clinical efficacy of radiofrequency ablation in high-risk patients with localized renal cell carcinoma and to assess the limitations of glomerular filtration rate in post-ablation renal function assessment.

Materials and methods. This single-center retrospective cohort included 24 patients with localized renal tumors treated with radiofrequency ablation between 2008 and 2019 at the Zaporizhzhia Regional Antitumor Center. Indications comprised solitary kidney (n = 5), bilateral tumors (n = 3), and local treatment in the setting of recurrent or metastatic disease (n = 18); categories were not mutually exclusive. A percutaneous approach was used in 21 (87.5 %) patients, laparoscopic in 1 (4.2 %), and open in 2 (8.3 %). Core-needle tissue samples from macroscopically intact parenchyma adjacent to the ablation zone were obtained intraoperatively and 72 hours after ablation. Immunohistochemical analysis of CD34 and HIF-1α expression was performed and correlated with estimated glomerular filtration rate. The Wilcoxon signed-rank test was used for statistical evaluation.

Results. Complete tumor necrosis was observed in 75–100 % of cases. Most complications were minor (Clavien–Dindo I–II: 29.2 %), while serious adverse events (IIIa–IV) occurred in three patients (12.5 %). The mean hospital stay was 3.0 ± 0.8 days. Clear cell carcinoma was the predominant histology – (83.3 %), with papillary carcinoma in 16.7 %. Tumor size ranged from 2.1 cm to 4.0 cm (mean 3.2 ± 0.5 cm); 37.5 % of patients had lesions >3 cm. Postoperative immunohistochemistry showed a significant decrease in CD34 expression (100 ± 15 vs. 58 ± 12; p = 0.014) and an increase in HIF-1α levels (25 ± 8 vs. 78 ± 14; p = 0.008) despite a stable estimated glomerular filtration rate (62.4 ± 7.8 mL/min/1.73 m^2 vs. 61.9 ± 8.1 mL/min/1.73 m^2, p = 0.74).

Conclusions. Radiofrequency ablation is an effective nephron-sparing option for high-risk patients with localized renal cell carcinoma. However, stable estimated glomerular filtration rate values may mask subclinical parenchymal injury; tissue-level biomarkers capture structural and microvascular alterations. These findings support prospective validation.

Keywords: renal cell carcinoma, glomerular filtration rate, immunohistochemistry, minimally invasive surgical procedures, radiofrequency ablation.

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Поза межами клубочкової фільтрації: гістологічне оцінювання ушкодження ниркової тканини після радіочастотної абляції при локалізованому раку нирки

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Мета роботи – оцінити клінічну ефективність радіочастотної абляції в пацієнтів із локалізованим нирково-клітинним раком і вираженою супутньою патологією, а також проаналізувати обмеження використання швидкості клубочкової фільтрації як індикатора збереження функції нирок після лікування.

Матеріали і методи. Здійснили ретроспективний аналіз 24 пацієнтів із локалізованим нирково-клітинним раком, яким виконано радіочастотну абляцію у 2008–2019 рр. на базі Запорізького обласного клінічного онкологічного диспансеру. Головні показання – єдина нирка (n = 5), двобічні ураження (n = 3), рецидив чи метастатичне ураження (n = 18); категорії не виключали одна іншу. Перкутанний підхід застосовано у 21 (87,5 %) пацієнта, лапароскопічний – в 1 (4,2 %), відкритий – у 2 (8,3 %) випадках. Зразки тканини (біоптати) з інтактної паренхіми, прилеглої до зони абляції, отримували інтраопераційно та через 72 години після втручання. Експресію CD34 і HIF-1α оцінювали імуногістохімічно та зіставляли з показниками швидкості клубочкової фільтрації. Статистичний аналіз – критерій знакових рангів Вілкоксона.

Результати. Ступінь некрозу в зоні абляції становив 75–100 %; у доступних для морфологічної верифікації випадках підтверджено повний некроз. Переважали випадки світлоклітинної карциноми – 83,3 %, папілярної – 16,7 %. Середній розмір пухлини – 3,2 ± 0,5 см. Ускладнення ступеня I–II за Clavien–Dindo зареєстровано у 29,2 % випадків; тяжкі (IIIa–IV) – у 3 (12,5 %) пацієнтів. Тривалість госпіталізації – 3,0 ± 0,8 доби. Після абляції в інтактній паренхімі нирки виявлено статистично значуще зниження екс-

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пресії CD34 (100 ± 15 порівняно з 58 ± 12, p = 0,014) та підвищення HIF-1α (25 ± 8 порівняно з 78 ± 14, p = 0,008) на фоні стабільної швидкості клубочкової фільтрації (62,4 ± 7,8 мл/хв/1,73 м^2 порівняно з 61,9 ± 8,1 мл/хв/1,73 м^2, p = 0,74).

Висновки. Радіочастотна абляція є ефективною нефрон-зберігальною опцією для лікування локалізованої нирково-клітинної карциноми у пацієнтів із супутньою патологією. Водночас стабільна швидкість клубочкової фільтрації не виключає наявності субклінічного ушкодження паренхіми. Імуногістохімічні маркери CD34 і HIF-1α можуть бути використані для виявлення мікроскопічних структурних змін після втручання. Результати обґрунтовують доцільність подальших проспективних досліджень.

Ключові слова: нирково-клітинна карцинома, швидкість клубочкової фільтрації, імуногістохімія, малоінвазивні хірургічні втручання, радіочастотна абляція.

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The treatment paradigm in oncology has moved from an exclusive pursuit of cure to patient-centered care that emphasizes quality of life [1]. This evolution is particularly relevant to the management of localized renal cell carcinoma (RCC), where therapeutic strategies must balance oncologic control with comorbidities and long-term renal preservation [2].

Advances in imaging modalities – including ultrasound, computed tomography, and magnetic resonance imaging – have markedly increased the incidental detection of small renal masses, especially cT1a tumors. Early diagnosis enables timely, less invasive interventions such as nephron-sparing surgery or thermal ablation, often before metastatic spread occurs. A recent systematic review in Lancet Oncology comparing stereotactic body radiotherapy, radiofrequency ablation (RFA), microwave ablation, and cryoablation for localized RCC reported 5-year local control rates of 92 % for RFA (95 % CI: 88–96), with a low incidence (2 %) of grade 3–4 complications across all techniques [3].

Notably, despite their localized appearance, approximately 2 % of cT1a RCCs present with synchronous metastases – most commonly to bone and lung – emphasizing the urgency of effective early intervention [4].

For patients with high surgical risk, RFA has become a viable, minimally invasive alternative. Recent data by Singh et al. demonstrated favorable oncologic outcomes (78.6 % 3-year recurrence-free survival) and stable glomerular filtration rate (GFR) following RFA in a high-risk cohort, supporting its intermediate-term efficacy [5]. However, treatment outcomes are often assessed by GFR – a global marker reflecting the combined function of both kidneys – which may obscure localized injury in the treated renal unit.

Beyond this anatomical limitation, GFR is influenced by factors such as age, sex, race, and hydration status, introducing substantial interindividual variability [6]. In the context of RFA, this is particularly problematic: thermal necrosis, ischemia, intravascular coagulation, and apoptosis may occur without evident changes in systemic GFR [7]. Consequently, significant structural injury may go undetected despite stable laboratory parameters.

To address this gap, we employed immunohistochemical markers – CD34 and HIF-1α – as tissue-level biomarkers to evaluate the integrity of preserved renal parenchyma after ablation. CD34 is an established indicator of microvascular density and endothelial health, while HIF-1α serves as a surrogate for hypoxia-induced cellular stress [8]. Notably, a recent comprehensive review has highlighted the pivotal role of HIF-1α in the pathobiology of clear cell RCC, including its influence on angiogenesis, proliferation, and metabolic adaptation – underscoring the rationale for its use in this context [9].

Combining immunohistochemistry-derived tissue biomarkers provided a more precise, localized, and biologically meaningful assessment of renal parenchymal viability, revealing subclinical injury that conventional global functional measures may miss.

Aim

To evaluate the clinical efficacy of radiofrequency ablation in high-risk patients with localized renal cell carcinoma and to assess the limitations of estimated glomerular filtration rate for post-ablation renal function assessment.

Materials and methods

This retrospective analysis included 24 patients with localized renal cell carcinoma who underwent RFA between 2008 and 2019 at the Zaporizhzhia Regional Antitumor Center. Despite the extended study period, all procedures were conducted according to a standardized institutional protocol to ensure methodological consistency. Written informed consent was obtained from all participants, in accordance with institutional and international ethical standards.

The cohort consisted of 14 (58.3 %) men and 10 (41.7 %) women, aged 41–85 years (mean ± SD: 63.0 ± 5.2; median: 67.0). Indications for RFA included a solitary kidney (n = 5), bilateral renal tumors (n = 3), and local recurrence or metastatic disease (n = 18). All patients had significant comorbidities precluding surgical resection.

RFA was performed using the Cool-tip RF system (Covidien™, Dublin, Ireland). Percutaneous access under ultrasound guidance was used in 21 cases (87.5 %), while laparoscopic and open approaches were employed in 1 (4.2 %) and 2 (8.3 %) patients, respectively. Energy delivery parameters were individualized based on tumor characteristics (size, location, vascularity) as determined by preoperative imaging.

Tissue samples were obtained intraoperatively and at 72 hours post-RFA from macroscopically intact renal cortex located 1.5–2.0 cm from the ablation zone, ensuring sampling from comparable regions. Samples were formalin-fixed, paraffin-embedded, and stained with antibodies

Table 1. Clavien–Dindo classification of postoperative complications in the RFA cohort

Clavien–Dindo grade	Complication type	n (%)
I–II	Postoperative pain, pyelonephritis, perinephritis	7 (29.2 %)
IIIa	Pneumothorax (not requiring general anesthesia)	1 (4.2 %)
IIIb	Thermal colonic injury (requiring general anesthesia)	1 (4.2 %)
IV	Acute kidney injury	1 (4.2 %)
V	–	0 (0.0 %)

Table 2. Comparison of CD34 and HIF-1α expression levels before and after RFA

Marker	Pre-RFA (mean ± SD)	Post-RFA (mean ± SD)	P-value
CD34	100 ± 15	58 ± 12	0.014
HIF-1α	25 ± 8	78 ± 14	0.008

against CD34 (clone QBEnd/10, Dako, Agilent Technologies, USA) and HIF-1α (clone H1alpha67, Novus Biologicals, USA). Immunohistochemical staining was visualized with the EnVision™ FLEX system and DAB chromogen. All microscopic evaluations were performed with an Olympus BX43 microscope.

CD34 expression was quantified as microvessel density in five randomly selected high-power fields (400×), while HIF-1α staining intensity was graded semi-quantitatively on a 0–3+ scale. Quantitative image analysis was performed using ImageJ software (NIH, USA).

Postoperative follow-up included ultrasound at 2, 4, and 8 weeks to monitor the ablation zone and evaluate fibrosis. All ultrasound and pathological assessments were conducted by board-certified specialists. Complications were classified according to the Clavien–Dindo grading system. Perioperative management adhered to institutional Enhanced Recovery After Surgery protocols.

Clinical data were extracted from institutional records, including outpatient charts (Form No. 003/o) and inpatient medical records (Form No. 025/o).

Normality of continuous variables was assessed using the Shapiro–Wilk test. Pre- and post-RFA biomarker values were compared using the Wilcoxon signed-rank test. All analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA), under an institutional academic license. A two-tailed p-value <0.05 was considered statistically significant.

The study was approved by the Bioethics Committee of Zaporizhzhia State Medical and Pharmaceutical University (approval No. 9; 29 August 2025) and conducted in accordance with the Declaration of Helsinki and applicable regulations. Clinical interventions performed in 2008–2019 constituted standard care; the Committee granted a waiver of additional informed consent for the retrospective analysis of de-identified data. Prior ethical oversight was provided by the Ethics Committee of the State Institution "Zaporizhzhia Medical Academy of Postgraduate Education of the Ministry of Health of Ukraine" (approval No. 3, 12 December 2022).

Results

RFA was technically successful in all 24 patients, with no intraoperative failures. The percutaneous approach was used in 21 (87.5 %) patients, while laparoscopic and open approaches were employed in 1 (4.2 %) and 2 (8.3 %) cases, respectively. The mean procedure time was 60 minutes for percutaneous RFA and 120 minutes for laparoscopic or open approaches. Blood loss remained minimal in all groups, and no conversions to open surgery were required.

Histological confirmation of RCC subtype was achieved in all patients, either via intraoperative frozen section or preprocedural core biopsy. Clear cell carcinoma was the predominant subtype (n = 20, 83.3 %), followed by papillary RCC (n = 4, 16.7 %). Tumor size ranged from 2.1 cm to 4.0 cm (mean 3.2 ± 0.5 cm), with nine patients (37.5 %) presenting with lesions >3 cm. Exophytic tumors with >25 % protrusion into the perinephric fat demonstrated the highest ablation efficacy, with complete necrosis observed on follow-up imaging in all such cases.

Ultrasound follow-up at 2, 4, and 8 weeks showed an avascular ablation zone with stabilization or reduction in lesion size, consistent with complete necrosis. To minimize interobserver variability, all ultrasound examinations were conducted by the same experienced radiologist.

The mean length of hospital stay was 3.0 ± 0.8 days – significantly shorter than the institutional historical average for open partial nephrectomy (7.0 ± 1.5 days) – reflecting the benefits of minimally invasive techniques and adherence to enhanced recovery protocols.

Postoperative complications are summarized in *Table 1*. Postoperative immunohistochemical analysis demonstrated a statistically significant reduction in CD34 expression (mean: 100 ± 15 vs. 58 ± 12, p = 0.014), alongside a pronounced increase in HIF-1α levels (25 ± 8 vs. 78 ± 14, p = 0.008). These changes are indicative of endothelial injury and hypoxia-induced stress in the preserved renal cortex. Notably, these alterations occurred despite stable systemic renal function, as measured by estimated glomerular filtration rate (eGFR) *(Table 2)*.

eGFR remained stable before and after the procedure (pre-RFA: 62.4 ± 7.8 mL/min/1.73 m^2 vs. post-RFA: 61.9 ± 8.1 mL/min/1.73 m^2, p = 0.74), reinforcing the hypothesis that global renal function may fail to reflect localized, subclinical injury.

The selection of CD34 and HIF-1α as tissue-level biomarkers was based on their validated diagnostic relevance in models of renal ischemia. CD34 is a reliable indicator of microvascular density and endothelial integrity (sensitivity >85 %), while HIF-1α serves as a central regulator of hypoxia-induced angiogenesis and metabolic adaptation. This dual-marker strategy enables a more precise, localized assessment of renal injury – one that is not captured by conventional serum-based indicators.

Collectively, these findings emphasize the limitations of relying solely on global functional metrics and suggest a valuable role for immunohistochemistry in detecting silent or evolving injury, particularly in anatomically complex or high-risk patient populations.

Discussion

RFA has gained increasing recognition as a nephron-sparing treatment option for patients with localized RCC ≤4 cm. Our findings support its short-term safety and efficacy, particularly in carefully selected individuals. These observations are consistent with the study by R. K. Singh et al., which demonstrated a 78.6 % three-year recurrence-free survival and preserved renal function in surgically unfit patients with small renal masses treated with RFA [5].

However, a deeper tissue-level analysis reveals that RFA, despite its minimally invasive nature, carries underappreciated risks that may not be visible under current clinical evaluation standards. While GFR remains the prevailing benchmark for assessing renal function post-intervention, our findings contribute to growing evidence that this parameter may be insufficient for detecting localized renal damage. Specifically, our immunohistochemical analysis revealed significant postoperative ischemia and microvascular injury in the preserved renal parenchyma, as evidenced by decreased CD34 expression and elevated HIF-1α levels. These changes were observed despite stable systemic GFR values, underscoring a disconnect between conventional functional assessments and true tissue viability.

Notably, these biomarker alterations may carry broader implications beyond functional underestimation. Recent evidence suggests that inadequate thermal exposure during RFA can activate pro-oncogenic pathways at the periphery of the ablation zone. Sublethal heating has been shown to induce HIF-1α and vascular endothelial growth factor, promoting angiogenesis and potentially contributing to tumor recurrence. Additionally, upregulation of the AKT and c-Met signaling pathways, along with epithelial-mesenchymal transition, has been associated with increased tumor proliferation, survival, and metastatic potential [10]. These molecular events underscore the oncologic risks associated with incomplete ablation and reinforce the importance of precise energy delivery and tissue-level evaluation to avoid subtherapeutic exposure in critical zones.

Importantly, our results highlight a critical mismatch between apparent functional preservation and the underlying biochemical reality. Patients may exhibit stable global renal parameters while silently accumulating subclinical injury in the treated renal unit. This finding challenges the sufficiency of current follow-up protocols and prompts reconsideration of how we define the therapeutic success of minimally invasive interventions.

Although the overall complication rate in our cohort was low, the presence of Clavien–Dindo grade III–IV events – including thermal injury to adjacent structures – confirms that RFA is not without serious risk. This is particularly important considering that repeated ablations are often necessary to achieve oncologic outcomes comparable to partial nephrectomy. In this regard, a multicenter study by M. E. Abdelsalam et al. demonstrated that RFA following prior partial nephrectomy achieved excellent long-term disease control, with a five-year overall survival of 93.1 % and recurrence-free survival of 94.4 %, along with a low Clavien–Dindo grade III complication rate of 3.7 % [11].

Further supporting this approach, Chan et al. compared image-guided ablation (RFA and cryoablation) to laparoscopic partial nephrectomy in patients with T1 RCC and reported equivalent long-term oncologic outcomes (hazard ratio for local recurrence with RFA: 0.04; 95 % CI: 0.03–0.48), alongside significantly better preservation of eGFR post-ablation (p < 0.001 for T1a; p = 0.047 for T1b) [12]. A meta-analysis comparing energy modalities in RCC ablation concluded that microwave ablation had lower local recurrence rates and shorter procedural times than cryoablation, suggesting that technical variables may influence reintervention rates and long-term renal integrity [13].

Our findings are consistent with literature questioning the long-term oncologic equivalence of RFA compared to surgery, particularly in tumors exceeding 3 cm or those located in challenging anatomical sites. A comparative study by M. E. Abdelsalam et al. reported no significant differences in complication rates (p = 0.11) or local recurrence (p = 0.15) between patients with 3–4 cm versus <3 cm T1a RCC, treated with RFA. Both groups exhibited 100 % metastasis-free and cancer-specific survival [14]. Furthermore, a recent meta-analysis of seven studies with ≥5-year follow-up found no significant differences between RFA and partial nephrectomy in terms of recurrence (OR 1.22), progression-free survival (HR 1.26), or cancer-specific survival (HR 1.27). However, overall survival favored nephrectomy (HR 1.76), emphasizing the need for judicious patient selection [15]. These data support a growing consensus that tissue-level analysis – through biopsy, imaging, or molecular profiling – should be incorporated into post-ablation surveillance protocols, particularly for high-risk individuals.

In addition, chronic kidney disease remains a significant non-oncologic cause of morbidity and mortality among RCC survivors. Long-term cohort studies have shown that cardiovascular diseases eventually surpass RCC as the leading cause of death in this population [16]. These data highlight the critical need for robust strategies to preserve renal function. Given that global

GFR measurements may fail to detect localized parenchymal damage, incorporating tissue-level biomarkers such as CD34 and HIF-1α into post-treatment evaluations may offer a more accurate assessment of renal integrity and inform strategies to reduce the long-term burden of chronic kidney disease.

Limitations of this study include its retrospective design, small sample size, and single-center scope. Nevertheless, the integration of objective tissue biomarkers provides a novel lens for evaluating the impact of RFA and underscores the frequently overlooked burden of thermal ischemia in nephron-sparing oncology.

Conclusions

1. RFA is an effective nephron-sparing strategy for patients with localized RCC who are unsuitable for surgery, providing a minimally invasive alternative with low perioperative morbidity and compatibility with enhanced recovery protocols.

2. Systemic GFR alone is insufficient to assess true renal preservation after RFA, as it may fail to detect subclinical ischemic or microvascular injury.

3. Tissue-level evaluation using histological and molecular markers – particularly CD34 and HIF-1α – enables sensitive detection of microvascular compromise and hypoxia-induced cellular stress, thus offering a more accurate assessment of renal integrity post-ablation.

4. Integrating immunohistochemical analysis into both patient selection and outcome monitoring may enhance the precision of RFA indications and facilitate early detection of patients at risk for incomplete ablation or long-term functional decline.

5. These results have informed the design of a prospective study to refine selection criteria, optimize procedural parameters, and improve surveillance strategies for RFA and similar ablative modalities in localized RCC.

6. Overall, these findings support a paradigm shift toward tissue-level precision and individualized assessment, with the potential to redefine success metrics for minimally invasive oncology.

Prospects for further research. Previous comparisons of nephron-sparing modalities based solely on glomerular filtration rate have been prone to substantial methodological bias, potentially misrepresenting the true extent of postoperative functional loss. By incorporating direct histological and molecular assessment, our approach provides a more accurate measure of renal injury. Such evaluation may not only enable fair comparison of organ-preserving techniques by their impact on postoperative function, but also help re-evaluate current treatment strategies and refine clinical guidelines for patient selection and procedural planning.

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References

1. Sheikh-Wu SF, Anglade D, Downs CA. A cancer survivorship model for holistic cancer care and research. Can Oncol Nurs J. 2023;33(1):4-16. doi: 10.5737/236880763314
2. Young M, Jackson-Spence F, Beltran L, Day E, Suarez C, Bex A, et al. Renal cell carcinoma. Lancet. 2024;404(10451):476-91. doi: 10.1016/s0140-6736(24)00917-6
3. Huang RS, Chow R, Benour A, Chen D, Boldt G, Wallis CJ, et al. Comparative efficacy and safety of ablative therapies in the management of primary localised renal cell carcinoma: a systematic review and meta-analysis. Lancet Oncol. 2025;26(3):387-98. doi: 10.1016/S1470-2045(24)00731-9
4. Gür M, Wang L, Liu F, Puri D, Meagher MF, Javier-Desloges J, et al. Mortality risk in clinical T1a renal cell carcinoma (RCC) with synchronous metastasis (SM): A comparative analysis of National Cancer Database (NCDB). J Clin Oncol. 2025;43(5_suppl):513. doi: 10.1200/JCO.2025.43.5_suppl.513
5. Singh RK, Gideon M, Rajendran R, Mathew G, Nair K. Advancing Treatment Frontiers: Radiofrequency Ablation for Small Renal Mass – Intermediate-Term Results. J Kidney Cancer VHL. 2023;10(4):1-6. doi: 10.15586/jkcvhl.v10i4.303
6. Delanaye P, Cavalier E, Pottel H, Stehlé T. New and old GFR equations: a European perspective. Clin Kidney J. 2023;16(9):1375-83. doi: 10.1093/ckj/sfad039
7. Wang Z, Jiang Y, Huang W, Liu X, Shan Q, Wu Z, et al. Impact of thermal ablation/cryoablation treatment on prognosis among patients with kidney cancer: a SEER database-based cohort study. Eur J Med Res. 2025;30:391. doi: 10.1186/s40001-025-02592-6
8. Morey K, Nimkar S, Dalia S. Hypoxia-inducible factor-1α inhibition in renal cell carcinoma. Tumor Discov. 2024;3(4):4346. doi: 10.36922/td.4346
9. Strikic A, Kokeza J, Ogorevc M, Kelam N, Vukoja M, Dolonga P, et al. Differential expression of HIF1A and its downstream target VEGFA in the main subtypes of renal cell carcinoma and their impact on patient survival. Front Oncol. 2023;13:1287239. doi: 10.3389/fonc.2023.1287239
10. Mueller LE, Issa PP, Hussein MH, Elshazli RM, Haidari M, Errami Y, et al. Clinical outcomes and tumor microenvironment response to radiofrequency ablation therapy: a systematic review and meta-analysis. Gland Surg. 2024;13(1):4-18. doi: 10.21037/gs-22-555
11. Abdelsalam ME, Hudspeth TN, Leonards L, Kusin SB, Buckley JR, Bassett R, et al. Effectiveness of Thermal Ablation for Renal Cell Carcinoma after Prior Partial Nephrectomy. Eur Urol Open Sci. 2023;57:45-50. doi: 10.1016/j.euros.2023.08.005
12. Chan VW, Osman FH, Cartledge J, Gregory W, Kimuli M, Vasudev NS, et al. Long-term outcomes of image-guided ablation and laparoscopic partial nephrectomy for T1 renal cell carcinoma. Eur Radiol. 2022;32(9):5811-20. doi: 10.1007/s00330-022-08719-1
13. McClure T, Lansing A, Ferko N, Wright G, Ghosh SK, Raza S, et al. A Comparison of Microwave Ablation and Cryoablation for the Treatment of Renal Cell Carcinoma: A Systematic Literature Review and Meta-analysis. Urology. 2023;180:1-8. doi: 10.1016/j.urology.2023.06.001

14. Abdelsalam ME, Awad A, Bassett RL, Lu T, Irwin D, Shah KY, et al. Technique and Outcomes of Radiofrequency Ablation of Biopsy-Proven 3-4 cm T1a Renal Cell Carcinoma. Biomedicines. 2025;13(6):1296. doi: 10.3390/biomedicines13061296
15. Li L, Zhu J, Shao H, Huang L, Wang X, Bao W, et al. Long-term outcomes of radiofrequency ablation vs. partial nephrectomy for cT1 renal cancer: A meta-analysis and systematic review. Front Surg. 2023;9:1012897. doi: 10.3389/fsurg.2022.1012897
16. Wang Z, Wang J, Zhu Y, Liu C, Li X, Zeng X. Cause-Specific Mortality Among Survivors From T1N0M0 Renal Cell Carcinoma: A Registry-Based Cohort Study. Front Oncol. 2021;11:604724. doi: 10.3389/fonc.2021.604724