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MEDICINE AND PHARMACY

Invisible scars: CD34 and HIF-1α in post-ablative renal tissue integrity

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A paradigm shift in localized renal cell carcinoma (RCC) management has placed long-term patient outcomes—rather than simple tumor eradication—at the forefront of clinical priorities (Sheikh-Wu et al., 2023; Young et al., 2024). This shift is especially pertinent as improvements in ultrasound, CT, and MRI have led to a marked rise in incidental detection of small renal masses (SRMs), especially cT1a tumors, in older patients with substantial comorbidities. Such cases highlight the demand for minimally invasive, nephron-sparing interventions, where the balance between oncologic control and functional preservation becomes paramount (Young et al., 2024; Huang et al., 2025).

Radiofrequency ablation (RFA) has become an established alternative for high-risk surgical patients, offering effective tumor control and lower perioperative morbidity. Recent meta-analyses show RFA achieves 5-year local control rates exceeding 90%, with major complications below 2% across ablative modalities (Huang et al., 2025). Still, approximately 2% of cT1a RCCs present with synchronous metastases—mainly to bone and lung—underscoring the need for precise and timely intervention (Gür et al., 2025).

Despite encouraging outcomes, there is growing recognition that systemic markers such as estimated glomerular filtration rate (eGFR) may overlook localized parenchymal damage post-ablation. GFR reflects global renal function, yet is influenced by patient demographics and comorbidities, often masking subclinical injury in the treated kidney (Delanaye et al., 2023). Our retrospective series from the Zaporizhzhia Regional Antitumor Center included 24 high-risk patients treated with RFA, all managed under a standardized protocol and in accordance with

international ethical guidelines.

The cohort comprised patients with a solitary kidney, bilateral tumors, or recurrent/metastatic disease, precluding surgical resection. Most RFA procedures were percutaneous under ultrasound guidance; a minority required laparoscopic or open approaches. Tumor sizes ranged from 2.1 to 4.0 cm, with exophytic growth patterns predicting superior ablation results. Tissue sampling from the renal cortex was performed intraoperatively and at 72 hours post-ablation to provide direct insight into parenchymal changes—an approach rarely adopted in clinical practice.

Histological confirmation identified clear cell RCC as the predominant subtype, with papillary variants in a minority. The mean hospital stay was three days, notably shorter than after open nephrectomy, highlighting the benefits of minimally invasive protocols. Complications were mostly minor and self-limiting, with serious adverse events limited to three patients—a rate in line with published series (Wang et al., 2025).

A cornerstone of this study was immunohistochemical assessment for subclinical injury post-RFA. CD34, reflecting microvascular density, and HIF-1α, a surrogate for hypoxia-induced stress and angiogenesis, were selected for their diagnostic value in RCC and ischemic injury (Strikic et al., 2023). Quantitative analysis demonstrated a significant reduction in CD34 and an increase in HIF-1α in the renal cortex adjacent to the ablation zone—changes that occurred despite stable eGFR and routine laboratory values.

These findings strengthen the argument that traditional global metrics such as GFR may grossly underestimate the true extent of microvascular and parenchymal damage following ablation (Delanaye et al., 2023; Wang et al., 2025). Molecular data now suggest that even sublethal heat at the ablation margin can activate oncogenic pathways, including VEGF, AKT, and c-Met, fueling angiogenesis and potentially contributing to recurrence (Strikic et al., 2023). Such evidence highlights the necessity for more nuanced, tissue-level evaluation in both clinical practice and research.

Over the long term, the implications of these “silent” injuries extend far beyond cancer control. Chronic kidney disease has emerged as a leading non-oncologic threat for RCC survivors, with cardiovascular mortality eventually outpacing cancer-related deaths (Wang et al., 2025). Because repeat ablations or further nephron-sparing interventions may be

necessary, accurate monitoring of true renal preservation becomes critically important.

Our results advocate for integrating immunohistochemical and molecular biomarkers into routine assessment of nephron-sparing therapies, especially for complex or high-risk patients. Tissue-level surveillance may help identify individuals at risk for progressive functional decline or incomplete ablation, thereby improving patient selection and procedural planning. This approach may also support the development of personalized monitoring protocols and next-generation strategies targeting the tumor microenvironment.

To conclude, while radiofrequency ablation remains an effective and well-tolerated nephron-sparing approach for localized RCC, exclusive reliance on conventional functional measures risks overlooking clinically significant injury. Direct tissue assessment with validated biomarkers such as CD34 and HIF-1α provides a more precise, individualized, and ultimately safer direction for minimally invasive renal tumor management.

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