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Modern risk assessment and prehabilitation in localized renal cell carcinoma

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Prehabilitation in localized renal cell carcinoma (RCC) is increasingly recognized as a critical adjunct to surgical planning, especially in patients with complex comorbid profiles. This approach transcends traditional perioperative protocols by integrating systemic, anatomical, and psychosocial dimensions into a unified, risk-adapted strategy that aligns with the realities of modern oncology.

Redefining Surgical Risk in RCC

Conventional risk stratification in RCC—focused largely on cardiopulmonary fitness, chronological age, and performance status—often fails to capture subtler, yet equally important, determinants of outcome: sarcopenia, malnutrition, cognitive impairment, prior abdominal interventions, psychiatric comorbidities, and hereditary syndromes. Each of these factors independently modifies perioperative risk and exerts a measurable impact on both oncologic and functional trajectories.

Sarcopenia and the Psoas Muscle Index (PMI)

Among these, sarcopenia remains critically underappreciated, particularly in RCC patients who may have a normal BMI. Robust evidence now links reduced skeletal muscle mass to increased postoperative complications, delayed recovery, and diminished survival. The psoas muscle index (PMI)—calculated as the combined cross-sectional area of both psoas muscles at the L3 vertebral level divided by height squared (m^2)—has emerged as a reliable surrogate for global muscle status.

PMI = Area of both psoas muscles at L3 (cm^2) / Height^2 (m^2)

CT- or MRI-based assessment of PMI enables early identification of occult frailty and guides prehabilitation

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protocols, including progressive resistance training, protein-optimized nutrition, and micronutrient correction. Though sex-specific cut-off values remain under investigation, low PMI consistently predicts higher 90-day morbidity and poorer oncologic outcomes (Cappe et al., 2022).

Multimorbidity: A New Paradigm in Risk Amplification

The majority of RCC patients present with multiple chronic conditions—hypertension, diabetes, chronic kidney disease, autoimmune or psychiatric disorders—that synergistically amplify surgical risk.

Hypertension is present in over 60% of cases, not only elevating RCC risk, but also accelerating CKD progression; each 10 mm Hg increase in blood pressure is associated with a 10-22% rise in RCC incidence (Kidoguchi et al., 2021). Diabetes mellitus impairs vascular integrity, delays wound healing, and heightens infection risk, underscoring the necessity of rigorous glycemic control (HbA1c ≤7%) and perioperative glucose management (140-180 mg/dL).

Crucially, the cumulative burden of multimorbidity is tightly linked to psychiatric morbidity. In a large cohort, patients with three or more chronic diseases had an eight-fold higher risk of clinical depression compared to those without comorbidities (Petrova et al., 2021). This interrelationship underscores the need for integrated mental health screening and support throughout the surgical journey.

Neuropsychiatric Comorbidities: The Hidden Risk Modifiers

Neuropsychiatric conditions—ranging from depression and anxiety to cognitive impairment and sequelae of stroke—are common in oncology populations and independently predict poor treatment adherence, longer hospitalization, and increased perioperative complications. Approximately one-third of hospitalized cancer patients fulfill diagnostic criteria for psychiatric disorders.

Best practice now advocates for routine preoperative psychiatric and cognitive evaluation, careful selection of renal-safe psychotropic regimens, and integration of cognitive-behavioral therapy (CBT) into perioperative care. Neuroanesthesia protocols, as well as structured psychosocial follow-up post-discharge, are crucial for optimizing recovery in vulnerable patients.

Autoimmune and Genetic Syndromes: Complex Surgical Landscapes

Patients with autoimmune diseases (e.g., lupus nephritis, rheumatoid arthritis) or hereditary syndromes (e.g., von

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Hippel-Lindau, ADPKD) present unique perioperative challenges—ranging from systemic inflammation and tissue fragility to the presence of multifocal or recurrent tumors. These individuals face increased risk of postoperative flare-ups, necessitating a combination of immunomodulatory strategies and individualized surgical planning. For small, slow-growing lesions (<3 cm), active surveillance is increasingly preferred, reducing unnecessary interventions and preserving organ function (Binderup et al., 2022). Novel targeted therapies, including JAK/STAT inhibitors, offer further opportunities to reduce perioperative risk in select cases.

Advanced Imaging and Surgical Precision in Anatomically Complex RCC

In anatomically complex scenarios—solitary kidneys, prior abdominal surgeries, or challenging tumor locations—advanced imaging modalities (3D CT, MRI, near-infrared fluorescence) and real-time intraoperative navigation have become essential. These technologies enable minimally invasive, nephron-sparing approaches that maximize tumor margin visualization, reduce ischemic injury, and optimize functional renal preservation. Their utility is particularly evident in central or multifocal tumors, anatomical variants, and patients with limited renal reserve (Cacciamani et al., 2020).

Practical Recommendations for Prehabilitation and Comorbidity Management in Localized RCC

Patient Group / Challenge	Clinical Risks & Considerations	Recommended Actions
Sarcopenia / Low Muscle Mass	Increased postoperative complications, delayed healing, underestimated risk.	Assess PMI at L3 level; tailored nutrition and preoperative physical training
Hypertension	Elevated risk of CKD, cardiovascular complications, RCC progression.	BP optimization (<130/80 mm Hg), nephroprotective medication review, lifestyle adjustments
Diabetes Mellitus	Infection risk, delayed wound healing, impaired renal recovery.	Preoperative HbA1c ≤7%, intra- and postoperative glycemic control, advanced wound management

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Table continuation

Multiple Comorbidities (Multimorbidity)	Higher complication risk, depression, reduced resilience.	Comprehensive multidisciplinary approach, regular depression screening, personalized prehabilitation
Autoimmune/Genetic Syndromes	Increased perioperative complications, renal vulnerability, risk of flare-ups.	Preoperative immunosuppression management, tailored surgical planning, genetic counseling, advanced imaging
Psychiatric/Neurological Disorders	Poor adherence, prolonged recovery, increased AKI risk.	Psychiatric assessment, nephro-safe medication selection, cognitive-behavioral therapy, vigilant AKI monitoring
Anatomical Complexity (e.g., after surgery)	Increased surgical difficulty, incomplete resection risk.	3D imaging preplanning, minimally invasive and robotic surgery, experienced surgical teams
Frailty / Advanced Age	High perioperative risks, slow recovery, susceptibility to multimorbidity.	Frailty screening, tailored prehabilitation, enhanced perioperative surveillance

Conclusion

Prehabilitation for localized RCC should be recognized as a core element of modern perioperative oncology care, extending well beyond traditional protocols. By systematically incorporating objective frailty metrics like PMI, tailoring management of comorbidities, leveraging advanced surgical imaging, and integrating neuropsychological and genetic insights, clinicians can meaningfully improve surgical safety, renal preservation, and patient quality of life. The future of RCC care lies in proactive, individualized strategies—delivered by multidisciplinary teams—capable not just of prolonging life, but of restoring resilience and wellbeing in a complex patient population.

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