·个人简介·

肿瘤肾脏病学的疾病表型、诊断评估与治疗管理前沿进展及展望

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［**摘要**］ 肿瘤肾脏病学作为肾脏疾病与肿瘤学交叉形成的新兴领域，近年来正经历从“被动应对肾损伤”向“主动整合肾保护”的模式转变。这主要是源于临床对肿瘤与肾脏之间复杂关系的认识不断深化，我们意识到肾脏不仅是肿瘤和抗肿瘤药物的被动受体，其功能状态本身也深刻影响着治疗决策的制订与患者预后。强调急性肾脏病（acute kidney disease，AKD）的概念，不仅弥补了急性肾损伤（acute kidney injury，AKI）与慢性肾脏病（chronic kidney disease，CKD）之间的“灰色地带”，也有助于更好的反映肿瘤患者肾损伤的特点。而随着新型抗肿瘤治疗的不断涌现，临床对肾脏安全的关注已从传统化疗药物的剂量限制性毒性，拓展至免疫检查点抑制剂、靶向治疗药物和嵌合抗原受体T细胞（chimeric antigen receptor T-cell，CAR-T）治疗相关肾损伤等全新表型的识别与管理。在这过程中，肾功能评估方法在肿瘤人群中的适用性也获得了系统性审视，以肌酐-胱抑素C联合公式和CamGFR v2为代表的新型估算模型正逐步填补传统评估手段的缺陷。尿液中新型生物标志物的出现，则为无创鉴别肾损伤病因提供了可能，有望减少不必要的肾活检并指导肾脏保护治疗的及时启动。国际肾功能不全抗肿瘤药物剂量调整指南（Integrating International Consensus Guidelines for Anticancer Drug Dosing in Kidney Dysfunction，ADDIKD）为肾功能不全患者的抗肿瘤药物剂量调整提供了框架，顺铂肾毒性的预防性干预等优化抗肿瘤方案也取得了新的循证证据。同时，液体活检、分子影像与人工智能辅助预警等新技术的融入，正在拓展肾脏健康评估的维度与精度。虽然近年肿瘤肾脏病领域在诊断治疗中均取得了显著进展，临床实践中仍面临着诸多挑战：多数新型生物标志物尚未在大型前瞻性肿瘤队列中得到充分验证，肾移植合并肿瘤等特殊人群的免疫治疗管理仍缺乏高质量证据，人工智能等模型也尚未在真实临床场景中检验其实际效用。未来，该领域的发展将更多依赖多组学数据与功能医学技术的深度融合，以及多学科协作管理体系的规范化建设，实现肾脏保护与肿瘤治疗的有效平衡。本文围绕肿瘤相关肾脏损伤的疾病表型、诊断技术以及治疗管理等方面进行综述，梳理该领域的最新进展及发展瓶颈，以期为优化临床实践与后续研究工作提供参考。

基金项目：上海市卫生健康委卫生行业临床研究专项（202640181）。
利益冲突：所有作者均声明无利益冲突。
伦理批件：
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引用本文：待补充。
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Funding: Shanghai Municipal Health Commission Health Industry Clinical Research Project（202640181）.
Conflicts of interest: All authors declare no conflicts of interest.
Ethical approval: . Not required.
Informed consent:
Cite this article:
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［**关键词**］ 肿瘤；肾脏病；免疫检查点抑制剂；细胞治疗；分子靶向治疗；化疗
中图分类号：R730.6；R692 **文献标志码：**A
DOI: 10.19401/j.cnki.1007-3639.XXXX.XX.001

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［**Abstract**］ Onconephrology, an emerging discipline at the intersection of nephrology and oncology, is shifting from a reactive approach to kidney injury toward proactive integration of renal protection. This shift reflects a deeper understanding of the bidirectional relationship between tumors and the kidneys: the kidney is not merely a passive target of the tumor itself and antineoplastic drug toxicity; rather, its functional status can significantly influence treatment decisions and patient outcomes. Emphasis on the concept of acute kidney disease (AKD) not only bridges the “gray zone” between acute kidney injury (AKI) and chronic kidney disease (CKD), but also better captures the distinctive characteristics of renal injury in cancer patients. With the rapid emergence of novel antineoplastic therapies, clinical attention to renal safety has expanded beyond the dose-limiting toxicities of conventional chemotherapeutic agents to encompass the recognition and management of entirely new phenotypes, including kidney

injuries associated with immune checkpoint inhibitors, targeted therapies, and chimeric antigen receptor T-cell (CAR-T) therapy. In parallel, the applicability of renal function assessment methods in oncologic populations has undergone systematic reappraisal. Newer equations, represented by the combined creatinine–cystatin C equation and CamGFR v2, are addressing the limitations of traditional assessment tools. The emergence of novel urinary biomarkers—such as CXCL9—offers the potential for noninvasive differentiation of kidney injury etiologies, potentially reducing unnecessary renal biopsies and facilitating timely initiation of renal protective strategies. The ADDIKD guidelines offer a framework for dose adjustment of antineoplastic agents in patients with renal impairment, and new evidence supports optimized strategies, including prophylaxis against cisplatin nephrotoxicity. Liquid biopsy, molecular imaging, and artificial intelligence (AI)-assisted early warning systems are also expanding the scope and precision of renal health assessment. Despite these advances, clinical practice still faces important challenges. Most novel biomarkers lack validation in large prospective oncologic cohorts.Management of immunotherapy in special populations, such as kidney transplant recipients with concurrent malignancies, remains unsupported by high-quality evidence. And the real-world utility of AI models has not been fully verified. Future progress in this field will depend on deeper integration of multi-omics data with functional assessment technologies and standardized multidisciplinary collaborative management, so that renal protection and oncologic therapy can be effectively balanced. This review summarizes recent advancements and identifies current bottlenecks in the disease phenotypes, diagnostic technologies, and therapeutic management of cancer-associated kidney injury , aiming to provide information for optimizing clinical practice and future research.

［**Key words**］tumors; kidney disease; immune checkpoint inhibitors; cell therapy; molecular targeted therapy; chemotherapy



伦理批件：不需要。
知情同意：不需要。
IIT研究备案：不需要。
Informed consent： Not required.
IIT Research Registration：Not required.

肿瘤肾脏病学是肾脏病学与肿瘤学交叉形成的新兴学科，关注恶性肿瘤及其相关治疗导致的肾损伤，以及慢性肾脏病患者并发肿瘤的风险与管理。肾脏与肿瘤之间存在双向而密切的流行病学联系。慢性肾脏病（chronic kidney disease，CKD）在癌症患者中非常普遍，肾功能不全与抗肿瘤药物系列研究（Renal Insufficiency and Anticancer Medications，IRMA）[1-2]显示，超过半数实体瘤患者估算肾小球滤过率（estimated glomerular filtration rate，eGFR）已低于90 mL/min/1.73 m²，其中12%-25%的患者处于eGFR < 60 mL/min/1.73 m²的中度及以上CKD阶段，且患病率随年龄增长而升高、因瘤种而异。同时肾功能下降本身也与肿瘤风险上升相关：纳入27项队列、超550万例参与者的荟萃分析[3]显示，eGFR <60 mL/min/1.73 m²人群的新发癌症风险较肾功能正常者升高约35%（IRR=1.35，95%CI：1.12~1.63），后续加拿大人群队列[4]进一步证实CKD患者的癌症死亡风险也显著增加。急性肾损伤（acute kidney injury，AKI）在肿瘤患者中同样是突出的负担，丹麦一项纳入120余万人的全国性队列[5]显示，癌症确诊后5年内AKI累积发生率达27%，其中以肾癌、肝癌与多发性骨髓瘤患者风险尤甚。另一方面，癌症本身即可影响肾功能和肾血流动力学，多中心对照研究[6]发现未经治疗的实体瘤患者基线eGFR反而高于同龄非肿瘤人群，提示肿瘤可能引起肾小球高滤过状态，而在随后的治疗过程中其eGFR年下降速率显著加快，这一发现为“肿瘤患者肾功能基线假象”提供了新的流行病学证据。

CKD和AKI不仅限制癌症患者的治疗选择与药物剂量调整，还与更高的死亡风险相关。因此，将精准、便捷的肾功能监测与积极的肾脏保护策略整合进肿瘤诊疗全程，通过多学科协作实现早期预防与干预，是改善患者整体预后的关键路径。本文围绕肿瘤肾脏病学的疾病表型、诊断技术、治疗策略与长期管理展开综述。

1 数据库收录文献的现状与进展

本文对国内外主要数据库进行检索，旨在探索肿瘤肾脏病学的疾病表型、诊断评估与治疗管理的前沿文献。其中，外文数据库包括PubMed、Embase、Cochrane Library、Web of Science，，中文数据库包括SinoMed、中国知网（CNKI）、万

方数据知识服务平台为检索源，检索时限为2020年1月1日至2026年7月31日，并追溯纳入文献的参考文献以补充早期经典研究。英文检索词包括“onconephrology”“cancer-associated kidney injury”“acute kidney injury”“acute kidney disease”“immune checkpoint inhibitor”“targeted therapy”“tyrosine kinase inhibitor”“glomerular filtration rate”“biomarker”等及其组合；中文检索词包括“肿瘤肾脏病学”“急性肾损伤”“免疫检查点抑制剂”“靶向治疗”“肾毒性”“生物标志物”等，以关键词/自由词为主进行检索。文献纳入标准为：（1）与肿瘤相关肾损伤的流行病学、诊断、治疗及管理相关的原始研究、系统评价、meta分析及指南/共识等；（2）语种为中文或英文。排除标准为：（1）仅能获得摘要而无法获取全文的会议摘要；（2）数据不完整或重复发表的文献；（3）与主题相关性低的个案报道（对罕见或重要不良反应、特殊诊疗决策等具有特殊临床参考价值的个案报告可酌情纳入）。证据取舍优先采用近年指南/共识、大型队列与随机对照试验，临床前研究仅用于机制阐述。文献检索、去重、标题或摘要初筛及全文复筛均由笔者独立完成，对存疑文献经反复阅读全文后确定是否纳入。经逐层筛选、追溯及补充相关文献，最终合计引用文献119篇。

3 肿瘤患者合并急性肾脏病（AKD）领域的研究进展

急性肾脏病（acute kidney disease，AKD）是持续时间不超过3个月的肾脏结构与功能异常。其概念即涵盖了定义明确的AKI（突发1-7天内的肾功能快速下降），也弥补了AKI至CKD（损伤持续≥3个月）之间的“灰色地带”，更加符合肿瘤患者较短时间内发生肾损伤的特点。在2026年第34届急性疾病质量倡议（Acute Disease Quality Initiative，ADQI）工作组共识[7]建议将抗癌药物导致的肾脏损伤命名为抗癌治疗相关AKD。大型外科队列的二次分析[8]显示，AKI后持续超过7天的肾功能异常与远期不良肾脏结局独立相关，提示肿瘤患者也应重视AKD后随访。随着新型抗肿瘤药物和细胞/基因/病毒治疗的不断涌现，更多因素与AKD相关，因此肿瘤患者合并AKD的临床表现、危险因素是肿瘤肾脏病学的研究热点之一。其病因构成较一般人群更为复杂，兼具普通内科病因与鲜明的肿瘤专科特征[9-10]，按发病机制和病变部位，可归纳为肾前性、肾小管间质损伤、肾小球损伤、肾脏微血管损伤及肾后性梗阻五类（表1）。

免疫检查点抑制剂（immune checkpoint inhibitor，ICI）相关急性肾脏病（ICI-AKD）已成为实体瘤领域最重要的肾损伤表型之一。汇总至2025年12月、纳入21项研究60799例患者的荟萃分析[22]显示，ICI-AKI的合并发生率为2.61%（95% CI：1.95%~3.28%），联合免疫检查点阻断方案下风险进一步上升。目前研究[23-25]报道的危险因素包括：较低的基线eGFR、合并基础慢性病、联合治疗方案、合并肾外其他免疫相关不良反应（immune-related adverse event，irAE）、以及联合应用质子泵抑制剂（proton pump inhibitors，PPI）、肾毒性抗生素、利尿剂等肾毒性药物暴露。ICI-AKD最常见的病理类型为急性间质性肾炎（acute interstitial nephritis，AIN），占比七成以上，但足细胞病、C3肾小球病等肾小球疾病以及血栓性微血管病（thrombotic microangiopathy，TMA）等亦有报道[26]。基于大规模药物警戒数据的分析[27]提示，不同ICI方案的肾脏风险也存在梯度差异：CTLA-4抑制剂的AKI报告风险可能高于PD-1/PD-L1抑制剂，而双免疫联合方案的风险最高（尤以PD-1+CTLA-4双免疫为甚）。ICI-AKD起病隐匿、缺乏特异性表现，既往研究[25]显示约2/3患者经规范治疗后可获完全或部分肾功能恢复，而肾功能未恢复者的死亡风险显著升高。

细胞治疗的广泛应用催生了新的肾损伤表型。嵌合抗原受体T细胞（chimeric antigen receptor T-cell，CAR-T）治疗相关AKI在各研究中报道[28]发生率为5%~33%，合并发生率为18.6%（95%CI：14.3%~23.8%），需肾脏替代治疗者合并发生率为4.4%（95%CI：2.1%~8.9%）。根据意大利一项单中心研究[29]，CAR-T治疗后发生AKI的患者均合并细胞因子释放综合征（cytokine release syndrome，CRS），其中重度CRS（3~4级）患者的AKI风险升高至16倍（OR=16.4，95%CI：1.9~138.5），提示高炎症状态及伴随的血流动力学改变、炎症性肾损伤等可能共同参与AKI发生。此外，也有报道提示基线eGFR降低与既往CKD史，低白蛋白血症，基线乳酸脱氢酶（lactate dehydrogenase，LDH）升高，前期肾毒性药物暴露及免疫效应细胞相关神经毒性综合征（immune effector cell-associated neurotoxicity syndrome，ICANS）等均为危险因素[30-31]，但不同研究队列结果存在一定差异。

表 1 肿瘤患者急性肾脏病的病因与临床特征

Tab. 1 Etiology and clinical features of acute kidney disease in tumor patients

Categories of causes	Main mechanism	Clinical scenarios	Clinical manifestations
Prerenal factors	Insufficient effective circulating blood volume	Chemotherapy-induced severe vomiting/diarrhea	Hypotension, poor skin elasticity, dry mucous membranes, oliguria
	Renal vasoconstriction and osmotic diuresis	Solid tumors with humoral hypercalcemia[11]	Polydipsia, polyuria, nausea, disturbed consciousness (severe cases)
	Perfusion disorders and renal congestion	Renal vein–inferior vena cava tumor thrombus; Tumor compression of major blood vessels	Lumbar swelling and pain, renal enlargement; Hematuria, proteinuria
Tubulointerstitial injury	Direct cytotoxicity	Chemotherapy such as cisplatin and ifosfamide[12-13]; NSAIDs; Contrast agents; Multiple myeloma	Non-oliguric AKI Renal enlargement; Renal tubular epithelial cell casts on urinalysis; Fanconi syndrome (light chain proximal tubular disease)[14]
	Intratubular obstruction (drug crystals; monoclonal immunoglobulin casts; crystalline deposition of purine metabolic end-product; calcium phosphate deposits)	High-dose methotrexate therapy[15]; Multiple myeloma[10,16]; Burkitt lymphoma; Acute leukemia chemotherapy; Extensive bone metastases (hypercalcemia)[16-17]	Drug crystals (crystalline nephropathy) and tubular epithelial cell casts on urinalysis; Rapid deterioration of renal function (myeloma cast nephropathy)[18]; Hyperkalemia, hyperphosphatemia, hyperuricemia (TLS); Altered consciousness, constipation, polyuria (hypercalcemia)
	Drug-induced T cell activation and infiltration of renal interstitial inflammatory cells	Immune checkpoint inhibitors therapy (PD-1/PD-L1/CTLA-4 inhibitors) [19]	Insidious onset; Hematuria; Often accompanied by extrarenal immune-related adverse reactions (rash, colitis, etc.)
	Diffuse renal interstitial infiltration of tumor cells	Lymphoma, leukemia (especially ALL, CLL), and multiple myeloma with plasma cell infiltration[10,16]	Renal enlargement (imaging); Progressive decline in renal function; Possible hematuria
Glomerular injury	Deposition of tumor-associated antigen-antibody immune complexes	Paraneoplastic glomerulopathy (membranous nephropathy associated with solid tumors)	Nephrotic syndrome; Renal injury can precede tumor diagnosis
	Podocyte injury, membranous nephropathy	Lymphoma; VEGF pathway inhibitors and TKIs, BCR-ABL inhibitors	Nephrotic syndrome
Microvascular injury	Endothelial cell damage; Inhibition of nitric oxide synthesis	VEGF pathway inhibitors therapy[20-21]	Proteinuria (nephrotic-range possible); Hypertension emergencies
	Complement activation-induced microvascular lesions	Directly caused by various tumors; Gemcitabine, mitomycin, platinum drugs	Thrombotic microangiopathy and hemolysis (anemia, thrombocytopenia, schistocytes)
	Formation of ADAMTS13 autoantibody	Proteasome inhibitors or interferons	Neurological symptoms; Significantly reduced ADAMTS13 activity in antibody-positive patients
Postrenal obstruction	Mechanical compression or direct invasion of the urinary tract	Compression of retroperitoneal/pelvic solid tumors; Enlargement of retroperitoneal metastatic lymph node	Oliguria or anuria; Renal colic or lumbar distension and pain; Dilated renal pelvis/ureteral effusion(imaging)

NSAIDs: Nonsteroidal anti-inflammatory drugs; AKI: Acute kidney injury; TLS: Tumor lysis syndrome; PD-1:Programmed cell death protein 1; PD-L-1: Programmed death-ligand 1; CTLA-4: Cytotoxic T-lymphocyte-associated protein 4; ALL: Acute lymphoblastic leukemia; CLL: Chronic lymphocytic leukemia; VEGF: Vascular endothelial growth factor; TKIs: Tyrosine kinase inhibitors.

4 肿瘤治疗前的肾脏评估与生物标志物的研究探索

4.1 肾脏健康评估：局限性与新模型开发

ADQI共识建议[7]肿瘤治疗前应对患者进行肾脏健康评估（kidney health assessment，KHA）。传统的肾功能评估主要依赖于eGFR的估算、血清肌酐及尿蛋白检测，这些方法在肿瘤人群中存在明显局限。血清肌酐受年龄、性别、肌肉量及肿瘤代谢状态等影响，在恶病质或化疗相关肌肉消耗患者中应用传统公式计算，结果可能高估肾小球滤过率，且肾小球超滤状态可能掩盖早期肾单位丢失[6, 10]；液体潴留与第三间隙积聚可进一步稀释肌酐浓度，造成AKD诊断延迟及抗肿瘤药物（尤其顺铂、甲氨蝶呤等化疗药）剂量决策失误。近年来，针对肿瘤人群的估算GFR的模型开发已取得进展，如CamGFR v2模型[32]，其在内部及多中心外部验证中的准确度与无偏性均优于CKD-EPI、MDRD、FAS及Lund-Malmö Revised等公式，但因仍以肌酐为唯一滤过标志物，无法摆脱肌肉量变化的根本制约，对不同种族、体型及肿瘤谱人群的适用性也仍需区域化校准验证。Titan等[33]在一项纳入

1145例血液及实体瘤患者的研究中发现，CKD-EPI肌酐-胱抑素C联合公式与实测GFR对比表现最优，基于此类证据，ADQI共识[7]建议，如能获得胱抑素C的检验结果，应优先采用CKD-EPI肌酐-胱抑素C联合公式进行评估，并在估算值不可靠或处于治疗决策临界值时推荐采用外源性标志物直接测量GFR。同时，2025年美国食品药品监督管理局（Food and Drug Administration，FDA）批准了经皮荧光检测外源性示踪剂（relmapirazin）实时GFR测量系统，这为床旁直接测量提供了新工具，但在肿瘤人群中的应用仍需进一步验证。除了肾小球滤过率计算，蛋白尿与尿沉渣分析也可提示肾损伤，却无法区分免疫介导、TMA或结晶沉积等具体机制。而肾活检病理诊断作为肾脏病诊断金标准，虽然其为侵袭性操作，有难以反复进行以动态监测疾病进展，在合并血小板减少或凝血异常的肿瘤患者中风险尤高等不足[19]，但为明确诊断仍建议有条件的患者接受肾活检。

4.2 新型生物标志物

AKI早期标志物涵盖肾小管损伤类（NGAL、KIM-1、NAG、L-FABP）、炎症修复类（IL-18、MCP-1、骨桥蛋白、CCL14）、滤过功能类（胱抑素C、脑啡肽原PenKid）及新兴候选（microRNA、suPAR、CHI3L1、SOD1）等类别，为肿瘤场景下的标志物组合选择提供了框架[34]。当前生物标志物研究正从单一指标验证转向多维度联合评估，根据在肿瘤人群中的验证成熟度（表2），临床可在不同场景下选择合适的标志物组合，其中功能评估（实测/估算GFR）与损伤监测（肾小管损伤标志物）并行仍是当前最优策略。

表2 肾损伤生物标志物在肿瘤人群的应用层级

Tab. 2 Application levels of kidney injury biomarkers in tumor populations

Levels	Representative markers	Core clinical application	Evidence status in tumor populations	Limitations
Clinically assistable	Cystatin C	Combined with creatinine for glomerular filtration assessment; Baseline renal function stratification and antitumor drug dosing reference	Recommended by KDIGO guidelines[35]; ASON 2024 Oncology Nephropathy Review supports prioritizing the use of creatinine－cystatin C combined equations for eGFR evaluation in cancer patients[36]	Reflects filtration function only and cannot identify early tubular injury; Affected by glucocorticoids, thyroid function, and tumor itself[37]; Cannot distinguish AKI etiology
Has promising clinical applications	CXCL9	Non-invasive differentiation of ICI-AIN from other cancer treatment-related AKI	Multicenter prospective tumor cohorts conducted; Strongest evidence in ICI populations[38]	Limited research on chemotherapy and CAR-T-related AKI; No unified threshold for cancer patients; Cannot replace kidney biopsy and is not recommended as a standalone diagnostic tool
	NGAL	Early detection of tubular stress injury. Auxiliary AKI monitoring	Multiple single-center tumor cohorts confirmed early elevation [39]	Diagnostic efficacy varies across studies; Low kidney specificity
	KIM-1	Assessing persistent proximal tubular injury; Monitoring chemotherapy-related tubular toxicity	Relatively sufficient evidence for chemotherapy-related renal injury[39];	Primary renal tumors may cause false positives; Limited data on ICI-related kidney injury; No unified reference threshold for cancer patients
	NAG	Detection of renal tubular lysosomal injury; Dynamic monitoring of chemotherapy and ICI nephrotoxicity; Pre-ICI early risk stratification	Supported by small sample single-center cohorts[40]	Unstable urinary enzyme activity; Easily affected by urinary tract infections and specimen contamination; Lack of standardized reference intervals for cancer patients

续表

Levels	Representative markers	Core clinical application	Evidence status in tumor populations	Limitations
	IL-18	Detection of tubular inflammatory damage; Early prediction of platinum-based chemotherapy-related AKI; Assessment of renal function and prognosis after kidney cancer surgery	Sufficient evidence for drug-induced and sepsis-related AKI; Small cisplatin cohort available[39]	Low kidney specificity; Lack of large-sample, multicenter validation
	Osteopontin (OPN)	Candidate markers for AKI-to-CKD transition and renal fibrosis	Small-sample validation cohort in cisplatin chemotherapy patients[41]	Solid tumors can secrete large amounts, making it difficult to distinguish whether the elevation originates from the kidney or the tumor
	L-FABP	Assessment of renal tubular oxidative stress injury; Monitoring platinum-based chemotherapy nephrotoxicity	Mainly animal experiments and transgenic model; Medium-scale prospective cohort validation for platinum-based chemotherapy patients[42]	Relatively small overall tumor cohort sample size; ICI-AKI evidence lacking; No multicenter external validation or dedicated diagnostic threshold
	MCP-1	Early prediction and diagnosis of AKI in cancer patients	Prospective cohort validation conducted, some reaching medium scale[43-44]	Easily affected by systemic inflammation; Lack of multicenter large-sample validation; Clinical applications not yet standardized
Needs validation in tumor population	TIMP2·IGFBP7 (NephroCheck)	Cell cycle arrest biomarker; Early risk warning of AKI	Sufficient evidence in general ICU-AKI and NephroCheck has been approved for clinical use;	Elevated baseline levels due to dehydration, proteinuria, and systemic inflammation in cancer patients; Inconsistent conclusions in oncology [45-46] General population cutoffs cannot be directly applied to cancer patients
	suPAR	Baseline chronic kidney risk stratification; Prediction of CKD progression after AKI	Extensive studies in general CKD and post-AKI fibrosis; Limited retrospective studies in tumor populations, mainly focusing on tumor prognosis	Tumor immune activation may elevate baseline levels
	CHI3L1 (YKL40)	Marker related to inflammation and renal fibrosis	Extensively studied in general fibrotic nephropathy; Mostly used as tumor burden marker in oncology	Serum levels mainly influenced by tumor burden; Lack of kidney injury-focused tumor cohorts
	microRNA	Marker of inflammation, cell death, and fibrosis; Early prediction of anti-tumor therapy-related AKI; Prognosis/efficacy prediction for renal cell carcinoma	Numerous animal experiments and small clinical trials in general kidney disease; Tumor kidney injury studies remain small-sample explorations[47]; Systematic review identified miR-34a and miR-21 as main candidate biomarkers and therapeutic targets[48]	Non-unified testing platforms ; Repeatability is poor; Standardized testing protocols yet to be established
	PenKid	Novel candidate peptide marker for tubular injury	Studies conducted in general population and critically ill patients[49];	Tumor-related human studies lacking Immature testing system . Validation in cancer patients remain unconducted
	CCL14	Chemokine marker predicting risk of AKI chronicity	Limited to AKI, renal fibrosis animal models and general severe AKI cohort[50]	Clinical evidence lacking in tumor-associated kidney injury
	SOD1	Candidate biomarker for oxidative stress-mediated kidney injury	Clinical validation in general population, sepsis, diabetes and other renal injury settings	No clinical basis for its application in tumor kidney injury

KDIGO: Kidney Disease: Improving Global Outcomes; ASON: American Society of Onconephrology; eGFR: Estimated glomerular filtration rate; AKI: Acute kidney injury; CKD: Chronic kidney disease; ICI: Immune checkpoint inhibitor; AIN: Acute interstitial nephritis; CAR-T: Chimeric antigen receptor T cells; CRS: Cytokine release syndrome; irAE: Immune-related adverse events.

在ICI相关肾损伤的诊断领域，生物标志物的探索近年取得新突破。Moledina等[51]通过尿液蛋白质组学分析发现，CXCL9是区分AIN与其他病因AKI的最强蛋白标志物，其在AIN患者中较对照组升高7.6倍（P=1.23×10^{-5}），外部验证队列中诊断AIN的曲线下面积（area under the

curve，AUC）达0.94（95% CI：0.86~1.00），且这种关联独立于年龄、性别、血肌酐、尿沉渣等临床指标（校正OR=6.0，95% CI：1.8~20）。该研究还指出TNF-α在AIN患者中较对照组也升高2.5倍（P=1.37×10^{-4}）。Farooqui等[52]的小样本前瞻性研究观察到尿液TNF-α区分ICI-AKD与其他病因的AUC达0.814（95% CI：0.623~1.000），并发现ICI-AKD组尿液IL-2和IL-10也显著升高（P<0.05）。这些研究为无创鉴别ICI-AIN提供了关键候选指标。随后Long等[53]采用高灵敏度核酸连接免疫夹心分析（Nucleic Acid-Linked Immuno-Sandwich Assay，NULISA）技术，对ICI治疗相关AKD患者的尿液和血浆样本进行深度蛋白质组学分析，证实尿液在区分ICI-AIN与非AIN病例方面较血浆更为敏感和特异。该研究不仅验证了CXCL9和TNF-α的诊断价值，还新发现IL-5、Fas、TNFSF4、CD274、IL-20、TNFSF15、TSLP、TREM1和CCL1等多种尿液标志物，其中IL-5与Fas联合构建的新型尿液标志物特征（IL-5+Fas）诊断ICI-AIN的AUC达0.94，优于该研究中所有其他单个标志物，显著提升了无创诊断的准确性。此外，其他候选标志物也被陆续报道，如尿可溶性PD-1（usPD-1）已有临床研究[54]提示其可有效鉴别ICI-AIN与急性肾小管坏死（acute tubular necrosis，ATN），外周血可溶性白介素-2受体（soluble interleukin-2 receptor，sIL-2R）则被发现在诊断ICI相关肾炎方面具有极高的准确性[55]。这些新型生物标志物有望减少不必要的肾活检，指导激素治疗的及时启动，并为ICI再挑战的决策提供依据，但目前仍需在大规模前瞻性肿瘤队列中进一步验证其临界值和临床效用。

4.3 液体活检、分子影像学与人工智能辅助

液体活检与分子影像学的整合正推动肾肿瘤与肾损伤评估的精细化。循环肿瘤细胞、循环肿瘤DNA联合多组学数据可构建肾癌的全局分子图谱，提升小肾肿块良恶性鉴别精度并指导个体化治疗[56]。可激活型近红外荧光探针与尿液生物正交报告系统，已在实验模型中展现出对抗肿瘤疗效及伴随肾损伤进行无创动态评估的潜力，为抗肿瘤药物肾毒性的早期可视化监测提供了新工具[57]。此外人工智能与机器学习也正加速渗透：基于电子病历的AKI早期预警已获肿瘤专科实证[58]。以英国Christie医院48 865例癌症治疗患者数据训练的随机森林模型可提前至多30d预测AKI事件，内部测试集AUC达0.881（95% CI：0.878~0.883），并在28 498例非肿瘤重症监护人群中完成外部验证（AUC 0.821，95% CI：0.820~0.821），提示其肿瘤来源模型具有一定的跨人群泛化能力，但此类模型的临床效用仍需前瞻性影响研究证实后才能扩大应用[58]。

5 治疗策略与长期管理的研究进展

5.1 根据肾功能的抗肿瘤药物剂量调整

肾功能不全在肿瘤患者中极为普遍，由于许多抗肿瘤药物及其活性代谢产物主要经肾脏排泄，当肾功能下降时，药物清除减慢、暴露量增加，这既可能加剧肾毒性，也可能导致骨髓抑制等非肾毒性不良反应加重。因此，基于肾功能的个体化剂量调整是肿瘤肾脏病学的核心临床实践之一。2025年发表的《国际肾功能不全抗肿瘤药物剂量调整指南》（ADDIKD）为这一领域提供了系统性指导框架。Sandhu等[59-60]阐述了将ADDIKD指南整合入日常实践的路径，在标准化肾功能评估（推荐优先使用实测GFR或估算GFR，而非传统的Cockcroft-Gault公式估算的肌酐清除率）及标准化肾功能分类（采用KDIGO的CKD分期系统）的基础上，强调需根据药物的药代动力学特征、药物剂量水平、治疗目标（治愈性与非治愈性）等进行分层管理。指南对59种抗肿瘤药物给出了基于证据联合临床实践经验的个体化给药推荐，主要选取甲氨蝶呤、顺铂、卡铂和纳武利尤单抗四种常用药，展示了其推荐与既往指南的差异。针对甲氨蝶呤大剂量（≥500 mg/m²）治疗，若为治愈性治疗且患者体能状态良好，eGFR在45~59 mL/min/1.73 m²者可维持全剂量，更低时则需根据eGFR估算值个性化减量；若为非治愈性或体能状态差，eGFR在45~59 mL/min/1.73 m²时即可考虑25%减量或换用替代方案，eGFR<45 mL/min/1.73 m²时则需减量50%或停用。顺铂的治疗策略推荐以eGFR<60 mL/min/1.73 m²为阈值，而当单次剂量> 50 mg/m²或因患者个体化差异eGFR估算不可靠时，需用实测GFR而非估算值指导初始剂量，且eGFR<45 mL/min/1.73 m²时应避免使用。卡铂的Calvert公式首选实测GFR（不按体表面积标准化）、不封顶于125 mL/min，但当eGFR在45~125 mL/min/1.73 m²或非治愈性治疗时，可用经体表面积调整的eGFR（CKD-EPI）替代；除非患者基线肾功能变化超过20%或临床状态发生显著改变，否则无需在每个化疗周期重新计算卡铂剂量，同时不推荐因肾功能不全降低目标AUC，

以免影响疗效。而纳武利尤单抗则不依赖肾脏清除，无需在肾功能不全时进行剂量调整，但需警惕免疫相关肾脏不良事件。

在指南推荐的其他的药物中[59]，主要经肾排泄的药物在治愈性治疗时，若肾功能损害尚不严重且具备监测条件，多数倾向足剂量治疗以保证疗效；在非治愈性治疗时，则需根据eGFR分层个性化减量，如达卡巴嗪、奥沙利铂在eGFR< 30 mL/min/1.73 m²时需减量，培美曲塞在30-45 mL/min/1.73 m²时即需考虑减量，而阿扎胞苷等少数药物可全程全剂量。主要经肝代谢的药物（紫杉类、蒽环类等），在轻中度肾功能不全时通常无需调整剂量，如多西他赛、多柔比星即使eGFR<60 mL/min/1.73 m²也推荐全剂量，极重度肾功能不全时则需多学科会诊。此外，对于接受连续性肾脏替代治疗（continuous renal replacement therapy，CRRT）或间歇性血液透析的患者，需根据药物分子量、蛋白结合率、分布容积及透析清除率进一步调整剂量与给药时机[61]。

现有的剂量调整建议多基于药代动力学模型或小样本研究，缺乏大型随机对照试验验证，未来需建立肿瘤人群专用的药物剂量调整数据库，整合治疗药物监测与临床结局，以完善临床决策循证依据。

5.2 化疗相关肾毒性的预防、解救与方案优化

以顺铂为代表的化疗药物作为一线的抗肿瘤药物，目前仍在广泛使用。其通过氧化应激和线粒体损伤等多种损伤机制产生剂量限制性肾毒性，充分水化、电解质监测与避免联用肾毒性药物仍是预防其肾损伤的基石[12]，具体方案应根据所用药物的不同个体化调整水化速率与尿液碱化程度。而方案优化的关键在于平衡疗效与肾保护，尤其应避免因轻度肾功能不全而武断排除适合化疗的患者。

针对特定药物的特异性解毒与防护是临床的重要补充。研究表明，顺铂化疗首日预防性应用镁剂可能通过补充镁离子、抑制肾小管摄取顺铂及抗氧化等机制，有效降低急性肾损伤及死亡风险。Gupta等[62]的多中心回顾性研究纳入13 719例首次顺铂化疗患者，其中28.4%（3893例）于首日接受静脉镁剂输注（中位剂量2g），镁剂组主要复合终点（14d内血肌酐倍增或需RRT，或死亡）发生率为2.7%，显著低于非镁剂组的5.3%，校正混杂因素后风险降低20%（aOR= 0.80，95% CI： 0.66~0.97）；同时次要终点90d主要不良肾脏事件（血肌酐升高≥1.25倍、肾脏替代治疗或死亡）的风险亦有所降低。该研究提示这项安全、廉价、可及性高的干预措施有望成为降低顺铂相关AKD风险的标准预防策略。大剂量甲氨蝶呤（HDMTX，≥1 g/m²）是血液肿瘤及实体瘤中枢神经系统预防的关键药物，而国内尚未上市的谷卡匹酶（羧肽酶G2，Glucarpidase）可将甲氨蝶呤水解为无活性代谢物，是其毒性反应的特异性解救药。国际共识[63]已明确谷卡匹酶的使用指征：对于输注时长≤24h的方案，当给药后24h甲氨蝶呤血药浓度>50 μmol/L、36h>30 μmol/L、42h>10 μmol/L或48h>5μmol/L，且血肌酐较基线显著升高，即应启用谷卡匹酶；若输注时长为36~42h，则当48h甲氨蝶呤浓度>5μmol/L时需考虑使用。2024年欧洲共识[64]已将其理想窗口从甲氨蝶呤给药后的48~60h提前至48 h内，超过60 h就会产生难以预防的不可逆毒性。随后Gupta等[65]的大规模多中心研究进一步证实，MTX-AKI患者中谷卡匹酶治疗与肾脏恢复显著相关（校正后OR=2.70，95%CI：1.69~4.31）。除此之外，亚叶酸也是甲氨蝶呤的有效解毒剂，但与谷卡匹酶应避免同时给药，而谷卡匹酶给药后48h内须采用色谱法监测甲氨蝶呤血药浓度。临床上其他特异性救护策略还包括，环磷酰胺/异环磷酰胺应联合美司钠预防出血性膀胱炎，以及对高危肿瘤溶解综合征（tumor lysis syndrome，TLS）患者使用别嘌醇或拉布立酶控制尿酸并视代谢情况碱化尿液[17]等。

除了上述成熟策略，许多探索性新干预已在动物模型证实。其作用机制包括：铁死亡抑制剂（如芦荟大黄素，可通过激活Nrf2通路并上调下游抗氧化和抗铁死亡基因表达发挥肾保护作用[66]）；纳米抗氧化剂（如pH响应型二氧化铈纳米颗粒及黑磷/二氧化铈复合纳米酶，可通过清除活性氧恢复线粒体功能，选择性保护肾小管[67-68]）；铂离子清除与转运抑制剂（如新型金属螯合剂GMDTC可直接螯合并转运清除蓄积在肾小管上皮细胞内的铂离子[69]，卡维地洛、西咪替丁及槲皮素聚合物胶束均可通过抑制肾脏OCT2转运蛋白减少顺铂在肾小管的蓄积[70-71]）；以及一些中药单体或复方也提供了有益线索（如芍药苷通过靶向上调TNFAIP3表达，可抑制顺铂诱导的程序性坏死和炎症反应[72]）。

5.3 ICI–AKD的诊治及肾移植患者ICI应用

与化疗药物明确的剂量—毒性关系不同，ICI相关肾损伤起病隐匿、缺乏特异性临床表现，

目前无任何单一临床特征能可靠区分ICI-AKD与其他病因AKD，诊断上应遵循“监测—排除—确诊”的路径[73]。患者治疗期间需定期监测血肌酐与尿常规，血肌酐升高者应在24~72h内复查，同时评估容量状态、尿沉渣与泌尿系影像，系统排除肾前性灌注不足、肾后性梗阻、感染、近期造影剂暴露及质子泵抑制剂、NSAIDs等合并用药及其他非ICI相关病因，欧洲肿瘤内科学会（European Society for Medical Oncology，ESMO）[74]、美国临床肿瘤学会（American Society of Clinical Oncology，ASCO）[75]与癌症免疫治疗学会（Society for Immunotherapy of Cancer，SITC）[76]指南均强调在启动激素治疗前尽可能排除其他病因，中国专家共识[77]也提出相同观点。而当病因无法解释肾功能恶化，或尿检提示肾小球性血尿、肾病范围蛋白尿等不典型表现时，应进一步排查ICI相关肾小球病与TMA，完善补体、抗中性粒细胞胞质抗体、ADAMTS13活性、乳酸脱氢酶、结合珠蛋白及外周血涂片等检查。肾活检仍是确诊的金标准，美国肿瘤肾脏病学会（American Society of Onconephrology，ASON）立场声明[78]建议KDIGO 2~3期AKI或疑似肾小球疾病者应请肾脏科会诊并尽早活检，活检不可行而临床高度怀疑者可先经验性激素治疗。尿液CXCL9、TNF-α等新型标志物（详见3.2）尚不足以替代活检。

已明确诊断或临床高度怀疑ICI-AKD的患者，应按不良事件通用术语评价标准（Common Terminology Criteria for Adverse Events，CTCAE）的irAE分级框架制定治疗决策：1级（血肌酐超过正常值上限但不超过1.5倍正常值上限）是否暂停ICI治疗各指南意见尚不统一，应每周监测肾功能并纠正可逆因素；2级建议暂停ICI，在排除其他病因后启动泼尼松0.5~1.0 mg·kg^{-1}·d^{-1}治疗，若5-7天内肾功能无改善，应考虑尽早行肾活检明确病理类型，并将激素加量至1.0~2.0 mg·kg^{-1}·d^{-1}；3~4级则建议永久停用ICI，予甲泼尼龙冲击后继以口服激素，总疗程通常4~8周，具体时长需个体化调整。经上述分级管理，多数ICI-AKD患者肾功能可获得改善，但仍有部分患者对糖皮质激素反应不佳。二线免疫抑制治疗目前仍无统一推荐剂量与疗程。人源化小鼠模型[79]揭示TNF-α阻断可显著减轻免疫检查点抑制剂相关肾炎的肾组织炎症，而既往病例系列研究[80]显示抗TNF-α药物英夫利西单抗用于激素难治或复发性ICI-AIN可获得较高的肾功能恢复率，提示针对特定细胞因子的靶向干预是潜在的挽救路径。同时，血清及尿液标志物（TNF-α/Cr、CXCL9/Cr）指导英夫利西单抗剂量调整的个案研究[81]，提示了标志物驱动治疗的可行性。2025年MD安德森癌症中心发表的55例活检证实Ⅲ/Ⅳ期ICI-AIN的单中心回顾性研究[82]中，一线激素联合英夫利西单抗较单用激素有效缩短了肾脏应答时间（HR=2.448，95%CI：1.292~4.638）；NanoString分析进一步证实肾组织TNF-α高表达与肾脏应答相关，这为TNF-α靶向治疗提供了转化医学依据。针对少见类型——ICI相关肾小球病的治疗，研究[83]提示可首先考虑利妥昔单抗，因激素治疗效果有限不应作为核心方案。

经治疗肾功能恢复至1级以下的患者，后续则面临ICI再挑战的评估，需按初次损伤严重程度、病理类型与肿瘤控制需求分层决策，可优先选择更换类别或单药方案，同时密切监测并避免联用质子泵抑制剂等药物。再挑战后，低危患者建议首月每周监测一次肾功能，此后2~3个月内每2周1次；中危患者首月每周需监测2次肾功能，此后3月内每周一次[84]。现有数据[22，73，85]显示再挑战后复发率约14%~20%，而TMA或3级以上肾损伤者一般不建议再挑战；对不宜再挑战的患者，应经多学科讨论更换为肾毒性较低的替代抗肿瘤方案。值得关注的是，现有研究[86]显示短期糖皮质激素治疗irAE未显著降低ICI的抗肿瘤效应，这为“肾—肿瘤双获益”的临床决策提供了一定依据。

肾移植受者（kidney transplant recipients，KTR）因长期处于免疫抑制状态，恶性肿瘤发生风险显著高于普通人群，在这一特殊群体中的应用ICI始终面临着挑战：免疫抑制剂可能削弱ICI的抗肿瘤效应，而ICI激活免疫系统后可能诱发急性移植肾排斥反应，导致移植肾功能丧失。2026年ADQI共识[7]认为，对肾移植受者使用ICI抗肿瘤治疗具有可行性。但这类患者发生T淋巴细胞介导和抗体介导排斥反应的风险高达30%~40%，在此基础上，共识强调在肾移植受者中启动ICI治疗前，必须通过共同决策仔细评估治疗的风险与获益，同时考量移植术后时间、供体特异性抗体的存在与否、既往排斥反应史、替代抗癌治疗的可及性以及患者自身偏好等多方因素，力求在肿瘤控制不佳的风险与移植物失功从而重返透析的风险之间取得平衡。针对免疫抑制方案的调整，共识提出可考虑在ICI治疗前增加

糖皮质激素剂量或重新启用激素，另一方面可将钙调磷酸酶抑制剂（calcineurin inhibitor，CNI）转换为哺乳动物雷帕霉素靶蛋白抑制剂（mammalian target of rapamycin，mTOR），以期在降低排斥风险的同时保留抗肿瘤效应。调整免疫抑制剂方案后，还应密切监测肾脏功能及自身免疫相关指标，及时发现排斥反应或肾损伤迹象。而应用ICI后一旦发生移植肾排斥，治疗策略需根据活检病理类型制定。甲泼尼龙冲击、抗胸腺细胞球蛋白、静脉免疫球蛋白、英夫利西单抗及血浆置换等多种方案均有报道[87]，但仍无统一方案。目前关于ICI在肾移植受者中的安全性数据仍不充分，ICI-AKD在这类患者中的最佳管理策略也不明确，亟需进一步研究填补这部分空缺。

5.4 靶向药物及靶免联合治疗的肾毒性管理

靶向药物治疗相关肾损伤多与靶点药理作用相关，且多数药物设有剂量递减等级，其诊断强调用药时相应表型的对应。血管内皮生长因子（vascular endothelial growth factor，VEGF）通路抑制剂相关肾损伤以高血压、蛋白尿为主要临床表现，肾活检可见肾脏局限性TMA与足细胞病/局灶节段性肾小球硬化（focal segmental glomerulosclerosis，FSGS）共存表型谱，用药前应行基线肾脏评估，治疗中应动态监测血压（起始阶段每周）与尿蛋白，尿常规蛋白尿≥2+时则应进一步定量确认，新出现蛋白尿者还需行UPCR测定[88]，并完善乳酸脱氢酶、结合珠蛋白、外周血涂片排查TMA，因其可仅累及肾脏而无溶血与血小板减少等全身表现[89]。表皮生长因子受体（epidermal growth factor receptor，EGFR）酪氨酸激酶抑制剂（tyrosine kinase inhibitors，TKIs）、*BCR-ABL*融合基因抑制剂可诱发急性肾小管坏死、近端肾小管功能障碍或间质性肾炎（可合并IgA肾病），其临床表现可与ICI-AIN相似，确诊依赖肾活检。此外，部分靶向药物（如聚腺苷二磷酸核糖聚合酶［poly（ADP-ribose） polymerase，PARP］抑制剂、克唑替尼）可通过抑制肌酐分泌或转运，出现血肌酐升高的“假性AKI”[90]，临床可借助胱抑素C进行鉴别，避免误判与不必要的停药。

针对靶向药物相关肾损伤的治疗，应遵循“暂停—减量—停药”的梯度管理。以使用VEGF抑制剂的患者为例，当出现2级以上蛋白尿或血压控制不佳时需暂停给药，恢复后视药物类别予以降低一个剂量等级或原剂量给药（贝伐珠单抗不推荐减量；仑伐替尼首次发生可原剂量恢复，第二次发生须减量），而当24h尿蛋白≥2 g时则已达到贝伐珠单抗、仑伐替尼等药物的说明书暂停阈值，需待患者蛋白尿缓解至阈值以下后方可恢复用药[89]；3-4级蛋白尿时也须按各药说明书标准停药，部分药物缓解后可在减量基础上重启[91]。在此框架中，蛋白尿与血压的控制是重要环节与指标。VEGF抑制剂相关蛋白尿在临床表现中多为尿液中小球性蛋白升高，借鉴《KDIGO肾小球疾病治疗临床实践指南》[92]中的一般性原则，可优先选择血管紧张素转化酶抑制剂（angiotensin-converting enzyme inhibitor，ACEi）/血管紧张素II受体拮抗剂（angiotensin II receptor blocker，ARB）类药物来治疗，不管是否合并高血压。而相关高血压也可优选肾素-血管紧张素-醛固酮系统（renin-angiotensin-aldosterone system，RAAS）抑制剂控制[88-89]，但有研究[93]显示整体血压控制的达标可能比药物类别选择更为关键。同时VEGF抑制可激活内皮细胞、减少一氧化氮（nitric oxide，NO）生成，进而增加内皮素-1（endothelin-1，ET-1）的释放，其他肾病背景的研究[94]已发现患者血浆中ET-1的升高与蛋白尿的严重程度呈现正相关，Nihei等[95]也指出基线血浆ET-1水平可用以预测贝伐珠单抗治疗后严重蛋白尿的发生风险，提示拮抗内皮素受体可能是VEGF抑制剂相关蛋白尿的有效防治手段。动物实验[96]印证了这一设想：在舒尼替尼处理的大鼠中，同步使用内皮素A型受体（endothelin receptor type A，ETA）抑制剂西他生坦可有效预防高血压与蛋白尿。然而尽管在糖尿病肾病[97]、IgA肾病[98-99]及FSGS[100]等其他背景下已有了内皮素受体拮抗剂有效降低蛋白尿的临床依据，其应用于VEGF抑制剂相关蛋白尿的有效性及安全性暂未获得临床检验。确诊TMA或肾病综合征者多数需永久停药[90]。肾功能未恢复或不宜重启者，可优先考虑更换为非VEGF通路的靶向药物（如mTOR抑制剂）或其他类别方案，由肿瘤—肾脏多学科团队权衡肿瘤控制需求后制定，不应为保肾而无限期延迟抗肿瘤治疗。部分情况下，若对同类药物有明确适应证，也可在同类间更换（如达沙替尼相关显著蛋白尿可换用尼洛替尼或伊马替尼）[101]。

随着ICI与抗血管生成靶向药物联合方案在肾细胞癌、肝细胞癌等瘤种中成为一线标准治疗，两类药物的肾脏毒性叠加问题也日益突出。

Kovalenko 等[102] 进行的一项比较 ICIs 单药与 ICIs 联合 VEGFi 抗癌治疗后不良事件的荟萃分析中，联合方案较 ICI 单药显著增加了任意级别蛋白尿的风险（RR=2.15，95%CI： 1.55~2.97）。而 Dukkipati 等[103] 开展的关于肾细胞癌抗癌治疗肾毒性的系统综述与荟萃分析显示，靶免联合方案治疗组的全级别蛋白尿发生率较 VEGF-TKI 单药也显著增高（OR=2.01，95%CI 1.58-2.26）。另有活检研究[104] 中，靶免联合治疗的病例 68.8% 呈现累及肾小球、肾小管间质及血管的混合性病理损伤模式，病理谱系广，这也提示两类药物肾毒性存在复杂的交互影响。联合用药时准确的毒性归因直接决定着临床决策，以蛋白尿和高血压为主的表现提示 VEGF 通路介导的内皮损伤，宜优先暂停靶向药物；而以 AKI 伴无菌性脓尿、合并肾外 irAEs 或活检免疫性病变为主时，则更多指向 ICI 相关损伤，应优先考虑按 5.3 节所述免疫路径处理，避免“停错药”而延误肿瘤治疗。对于归因不明、蛋白尿进展至肾病范围、血压难以控制或肾功能持续恶化的患者，应尽早行肾活检并请肾脏科会诊[89，105]。

5.5 中医药在靶免药物治疗相关肾损伤中的应用

中医药作为肿瘤综合治疗的重要组成部分，其在靶免药物治疗相关肾损伤的防治中的价值和安全性风险均需得到重视。含马兜铃酸类草药、雷公藤制剂及部分矿物类中药的肾毒性已有充分报道，肿瘤患者合并 CKD 或 AKD 时使用中药应严格甄别。在此背景下，部分中药在 ICI 相关肾损伤中已展现出初步临床证据。一项纳入 48 例患者的前瞻性随机研究[106] 显示，在糖皮质激素基础上联合芪归益肾汤，可进一步降低血尿素氮与血肌酐水平、改善估算肾小球滤过率，减轻 ICI-AKI 的严重程度。同时系统综述[107] 提示，黄芪等中药既可能通过调节免疫微环境增强 ICI 疗效，又可能缓解 irAE，呈现“增效减毒”的双向调节潜力。在靶向药物相关肾损伤中，中医药干预主要针对最常见的蛋白尿表型实施。2026 年发布的《原发性肝癌分子靶向药物相关蛋白尿中西医结合诊疗专家共识》[108] 推荐，黄葵胶囊连续治疗 12 周可明显降低阿帕替尼所致蛋白尿并改善肾功能；益肾健脾固精汤联合厄贝沙坦可显著改善 VEGF 通路抑制剂相关蛋白尿患者的 24h 尿蛋白定量与肾功能等。上述方案对靶免联合方案中的蛋白尿问题同样具有参考价值，但目前针对联合方案直接的中医药证据仍然缺乏。

此外，中医非药物治疗对肿瘤合并肾损伤患者也可具有一定效用。如针灸在 CKD 患者中显示出降低血肌酐、缓解瘙痒等症状的潜在获益[109]，但现有证据等级较低；八段锦等中医传统功法在乳腺癌患者术后康复中可改善生活质量、疲乏与心理状态[110]，可作为肿瘤患者肾功能受损期间症状管理与整体康复的辅助手段，但其对药物性肾损伤本身的防治作用尚无直接证据。

总体上，中医药在肿瘤治疗相关肾损伤应用中呈现证据初现但等级偏低的特点。现有证据多来自小样本、单中心研究，多局限于单一瘤种，缺乏标准化辨证方案与高质量随机对照试验，且中药与 ICI、靶向药物之间的代谢性相互作用尚不明确，其临床应用仍需在严密监测肾功能的前提下审慎开展。

5.6 细胞治疗 AKD 的防治

CAR-T 治疗相关 AKD 的防治策略需围绕其发病机制展开。CRS 是 CAR-T 治疗后发生 AKD 的核心驱动因素，高浓度细胞因子释放导致血管扩张、心输出量下降、血管通透性增加及第三间隙液体积聚，引起肾脏低灌注和急性肾小管损伤[111]。研究[31，112] 报道，AKD 常发生于输注后 7~10d，与 CRS 高峰时间吻合。此外，TLS 是另一重要致病途径，其根源在于肿瘤细胞被快速摧毁后内容物大量释放入血引发代谢危象。

具体的防治策略中，预防具有更重要的临床意义。除了治疗前应进行全面的 KHA，对高危患者，如基线肾功能减退、功能状态差、肿瘤负荷高者，在 CAR-T 输注后还应严密监测出入量、体重、电解质、药物水平及肾功能变化，谨慎管理液体平衡，避免使用肾毒性药物，并及时处理感染等情况。ADQI 共识[7] 建议长期随访中在 1 个月、3 个月、6 个月和 1 年的常规治疗后里程碑评估中纳入尿白蛋白与肌酐比值（urine albumin-to-creatinine ratio，UACR）和（或）尿总蛋白与肌酐比值（urine protein-to-creatinine ratio，UPCR）检测，当新发 UACR > 30 mg/g 或 UPCR > 200 mg/g 时应转诊至肾内科。及时有效地控制 CRS 可显著降低 AKI 的发生和严重程度，它强调早期识别与分级管理：1 级 CRS（发热）以对症支持为主，密切监测尿量、血肌酐及电解质；2 级及以上 CRS 伴低血压时，推荐静脉补液及血管活性药物维持肾脏灌注；2 级 CRS 伴持续发热或进展趋势时，则应考虑托珠单抗（IL-6 受体拮抗剂）8 mg/kg 静脉输注，必要时需重复给

药；而糖皮质激素可用于托珠单抗难治的重度CRS[113]。针对TLS，应在高危患者中实施标准预防措施，包括充分水化和降尿酸治疗等[17]。纠正低磷血症则可有效降低ICANS的发生率和症状持续时间[114]。

值得注意的是，CAR-T治疗前存在肾功能不全并非绝对禁忌。回顾性研究[111]提示CAR-T在中度肾功能不全患者中可谨慎实施，但相应的AKD风险也会增高，一旦发生即可能使临床预后恶化。因此对于中重度CKD患者，应在多学科团队评估后进行个体化决策，将肾保护理念整合入CRS全程管理。针对肾移植受者此类特殊群体，目前也已有成功使用CD19靶向CAR-T治疗移植后淋巴组织增生性疾病的报道[115]，但淋巴耗竭方案（尤其是氟达拉滨）的剂量调整、免疫抑制剂的优化以及排斥反应的监测等方面仍缺乏充分数据[116]。因此，未来仍需要更大规模的前瞻性研究来明确CAR-T相关AKD的最佳防治策略，同时应关注特殊人群的管理优化。

6 展　望

肿瘤与肾脏之间并非单向的“疾病—并发症”关系，而是一个互为因果的闭环：肿瘤本身及其诊治过程可损伤肾脏，而肾功能受损又反过来限制抗肿瘤方案的选择与强度，最终侵蚀肿瘤治疗的生存获益。因此面对肿瘤患者的肾功能损伤，鉴别诊断需同时覆盖肾前性因素、副蛋白沉积、肿瘤浸润、代谢性损伤与肾后性梗阻代谢性损伤等肿瘤本身病因；治疗相关风险的评估也应在药物暴露计算基础上，纳入肿瘤负荷与全身炎症状态等背景因素。

展望未来，精准医学时代的肿瘤肾脏病学存在几个潜在的重点方向：①功能精准医学技术的开发，借助患者来源类器官与器官芯片模拟肿瘤-肾脏互作，弥补静态分子特征预测肾毒性的缺口[117-118]，联合基因组、转录组、蛋白质组与代谢组数据构建肾损伤动态网络模型，优化风险分层与干预时机[119]；②诊断模式转化，生物标志物研究从单一指标效能对比，转向以临床问题为导向的联合检测策略，并在肿瘤人群中完成前瞻性验证；③多学科整合管理体系构建，诊疗思维由单纯的器官保护转向肾-肿瘤双获益的综合决策，推动肿瘤科、肾脏科、影像科与药学多学科协作规范化，将肾脏风险分层、风险匹配监测、结构化病因鉴别与慢性肾脏病分期管理融入抗肿瘤治疗全程。

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（收稿日期：XXXX-XX-XX 修回日期：XXXX-XX-XX）
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