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KDIGO 2025框架下IgA肾病中医药证据与治疗定位

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摘　要

目的：在KDIGO 2025治疗框架下综述中医药治疗IgA肾病(IgAN)的临床证据、可能机制、安全性及治疗定位，区分短期替代终点与长期肾脏结局。方法：采用证据导向的叙述性综述，围绕现代支持治疗、中医药临床证据、机制证据和安全性组织资料，并按随机附加治疗、活性对照、非随机比较和系统综述分层。结果：部分标准化制剂、复方或中西医结合方案在规范支持治疗基础上可降低短期蛋白尿，但背景治疗、制剂、剂量、对照和结局差异较大，长期eGFR及肾衰竭获益尚未证实。机制研究多来自动物、细胞、网络药理学和分子对接，不能证明人体因果疗效；产品质量、毒性和药物相互作用资料也不充分。结论：中医药宜作为规范治疗基础上的潜在辅助或探索性干预，不能替代具有明确适应证的循证治疗；未来需标准化制剂、一致背景治疗、长期随机附加试验和系统安全监测。

关键词

IgA肾病，KDIGO 2025，中医药，辅助治疗，循证医学

Traditional Chinese Medicine for IgA Nephropathy under the KDIGO 2025 Framework: Evidence and Therapeutic Positioning

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Abstract

Objective: To review the clinical evidence, possible mechanisms, safety, and therapeutic positioning of traditional Chinese medicine (TCM) for IgA nephropathy (IgAN) within the KDIGO 2025 treatment framework, distinguishing short-term surrogate outcomes from long-term kidney outcomes. Methods: An evidence-oriented narrative review was conducted around contemporary supportive care, clinical evidence for TCM, mechanistic evidence, and safety, with studies grouped as randomized add-on trials, active-comparator studies, non-randomized comparisons, and systematic reviews. Results: Some standardized products, compound formulas, or integrated Chinese and Western medicine regimens may reduce short-term proteinuria when added to standard supportive care. However, background treatment, products, doses, comparators, and outcome definitions vary substantially, and benefits for long-term eGFR or kidney failure have not been established. Mechanistic evidence is derived mainly from animal, cellular, network-pharmacology, and molecular-docking studies and cannot establish causal benefit in humans. Information on product quality, toxicity, and herb-drug interactions is also incomplete. Conclusions: TCM should be regarded as a potential adjunctive or exploratory intervention on top of standard supportive care. It should not replace evidence-based treatments with established indications. Future studies require standardized products, consistent background therapy, long-term randomized add-on trials, and systematic safety monitoring.

Keywords

IgA Nephropathy, KDIGO 2025, Traditional Chinese Medicine, Adjunctive Therapy, Evidence-Based Medicine

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1. 引言

IgA 肾病(immunoglobulin A nephropathy, IgAN)以肾小球系膜区 IgA 沉积为主要病理特征，临床表现和进展速度差异较大。持续蛋白尿和估算肾小球滤过率(estimated glomerular filtration rate, eGFR)下降与进展风险相关，但短期替代终点不能直接等同于长期肾脏获益[1]-[4]。KDIGO 2025 将 IgAN 治疗组织为减少致病性 IgA 及免疫复合物形成、控制既有肾单位损伤两条并行路径。中医药研究数量较多，但临床研究、机制研究和现代背景治疗之间缺乏统一框架，容易把生物学合理性误写成临床疗效。因此，有必要在现代标准治疗背景下重新梳理中医药证据，明确其可承担和不能承担的治疗角色。本文围绕临床获益、机制解释、安全性和研究设计进行叙述性综述。

2. 方法

本文采用主题导向的叙述性证据综述。资料按四个问题组织：第一，KDIGO 2025 及相关研究确立的现代治疗基线是什么；第二，中医药在附加治疗、活性对照和非随机比较中的临床增量效应是否一致；第三，人体、动物、细胞及计算研究分别能够支持何种机制判断；第四，制剂质量、安全性、药物相互作用和结局选择如何限制临床外推。对蛋白尿、血尿和短期 eGFR 变化等替代或中间结局，与慢性 eGFR 斜率、持续性 eGFR 下降、肾衰竭复合结局及长期安全性分开评价。不同研究设计不作无条件合并。

文献检索与筛选

本综述为叙述性证据综述。正式投稿前需依据作者保存的检索记录补充以下信息：检索数据库为：待作者确认：如 PubMed、CNKI、万方、SinoMed、Web of Science 或 Embase；检索时间范围为：待作者确认：起始日期–结束日期；核心中文检索词包括“IgA 肾病”“中医药”“中西医结合”“蛋白尿”“肾功能”等，英文检索词包括“immunoglobulin A nephropathy”“IgA nephropathy”“traditional Chinese medicine”“Chinese herbal medicine”“proteinuria”“estimated glomerular filtration rate”等，并根据数据库主题词和自由词组合。纳入主要包括成人或儿童 IgAN 患者的临床试验、队列研究、系统综述、指南及与中医药干预或机制相关的动物、细胞和计算研究；排除重复发表、无法确认研究对象或干预措施、会议摘要或未正式出版资料及与研究问题无关的文献。具体检索日期、最终筛选数量、是否采用双人独立筛选及分歧处理方式仍需依据实际操作记录补充。

3. 结果

3.1. KDIGO 2025 框架下的治疗基线

KDIGO 2025 要求根据进展风险实施优化支持治疗，并在适宜患者中选择疾病特异性干预。支持治疗包括生活方式和心血管危险因素管理，以及无禁忌证时使用最大耐受剂量的 ACEI 或 ARB；SGLT2 抑制剂、靶向释放布地奈德、内皮素受体拮抗剂、补体抑制剂及 B 细胞或浆细胞相关治疗，分别针对血流动力学、黏膜免疫、补体和异常抗体反应等环节[1] [2] [5]-[13]。这些治疗的证据强度并不相同，短期蛋白尿下降也不能脱离长期 eGFR 和肾衰竭结局解读。

现有研究提示，疾病特异性治疗正在从单一免疫抑制转向风险分层和多环节干预。例如，sparsentan 在 PROTECT 研究中较厄贝沙坦降低蛋白尿，且慢性 eGFR 斜率存在组间差异；靶向释放布地奈德的 NefIgArd 研究报告了两年时间加权平均 eGFR 差异；补体和 APRIL 通路药物也已显示蛋白尿或相关生物标志物变化[6] [7] [12] [13]。这些结果说明现代治疗基线正在变化，也意味着评价中医药时必须说明患者是否接受了充分的基础治疗，以及中医药带来的效应是否具有独立增量(见图 1)。

在现代治疗基线明确后，中医药的比较对象应是规范支持治疗或相同疾病特异性治疗背景，而不是未经说明的“常规治疗”。KDIGO 2025 将蛋白尿降至低水平和减缓 eGFR 下降作为风险管理目标，但不同研究对蛋白尿阈值、随访时间和基础治疗的定义并不一致[1] [2] [4]。若研究仅报告治疗前后差值，而未说明对照组、背景治疗和分析时间点，便不能判断观察到的变化是否来自中医药本身。

现代药物研究也提示，IgAN 治疗效果需要结合时间和结局解释。靶向释放布地奈德研究纳入优化 RAAS 阻断后仍有蛋白尿的成人，报告了两年 eGFR 差异，但同时存在类糖皮质激素相关不良事件；sparsentan 研究报告蛋白尿和慢性 eGFR 斜率结果，仍需结合其主动对照设计理解[6] [7]。因此，中医药研究不能只比较短期蛋白尿，还应说明是否在相同治疗背景下观察到持续的肾功能获益。

补体、BAFF 和 APRIL 等通路的临床研究进一步说明，生物标志物和替代终点的变化并不自动等同于临床结局改善。iptacopan 研究报告蛋白尿及补体相关指标变化，sibeprenlimab 研究报告蛋白尿和 Gd-IgA1 变化，但这些结果仍需结合更长期的 eGFR 斜率、肾衰竭复合终点和安全性评价[12]-[15]。中医药研究若仅报告炎症因子或免疫球蛋白变化，也应将其表述为药效或机制线索，而不是患者获益的替代证明。

支持治疗本身也会影响中医药研究的解释。RAAS 阻断可降低蛋白尿，但对肾衰竭等硬结局的证据确定性有限；DAPA-CKD 的 IgAN 亚组提示 SGLT2 抑制剂具有肾脏保护信号[5] [16]。如果中医药试验未统一 ACEI 或 ARB、SGLT2 抑制剂和血压管理，组间差异可能来自基础治疗不平衡，而不是研究药物的真实增量。



Figure 1. Treatment pathways and the positioning of traditional Chinese medicine in IgA nephropathy under the KDIGO 2025 framework
图 1. KDIGO 2025 框架下 IgA 肾病治疗路径与中医药定位

特殊临床情境也限制外推。快速进展性 IgAN 需要先排除感染、药物和继发性免疫复合物病因，并按快速进展性肾小球肾炎处理；儿童、妊娠、严重肾功能减退和移植后复发患者缺乏与普通成人同等强度的证据[1] [2]。中医药研究若未明确这些人群和排除标准，不能将普通成人结果直接扩展到高风险临床情境。

3.2. 中医药临床证据及其解释边界

为避免将“中医药”作为单一干预处理，本文选取黄葵、槐杞黄、雷公藤和益肾化湿颗粒作为代表性干预，分别考察研究设计、蛋白尿或 eGFR 信号、安全性与在 KDIGO 框架下的可能定位。表 1 用于呈现证据边界，不代表这些制剂具有可相互替代的疗效。

表 1 显示，代表性干预的证据不能合并为一个“中医药总体疗效”。黄葵有较大样本主动对照数据，但长期结局仍有限；槐杞黄和雷公藤主要提供短期或小样本信号；益肾化湿颗粒的研究支持在优化支持治疗基础上的短期附加效应。上述结果均不足以证明中医药能够替代 ACEI/ARB、SGLT2 抑制剂、靶向释放布地奈德或其他具有明确适应证的治疗[1] [2] [5]-[7] [17] [18]。

中医药临床研究涉及辨证复方、黄葵及相关制剂、雷公藤及相关制剂、槐杞黄益肾化湿等标准化产品，以及与现代治疗联合的方案。部分随机试验、活性药物对照研究和系统综述提示，附加中医药可能降低蛋白尿或改善血尿；但研究间处方、剂量、疗程、对照、基础治疗和结局定义差异明显，样本量和随访时间也不一致[17]-[27]。因此，研究结果更适合被解释为特定制剂或方案在特定人群中的信号，不能概括为所有中医药均具有确定疗效。

Table 1. Evidence and possible positioning of representative traditional Chinese medicine interventions in IgA nephropathy
表 1. 代表性中医药干预 IgA 肾病的证据与可能定位

干预措施	临床证据与研究设计	疗效信号	安全性与结局限制	KDIGO 框架下可能定位
黄葵 (*Abelmoschus manihot*)	多中心随机、双盲、双模拟、非劣效试验；1470 例；48 周；黄葵 2.5 g，tid vs 氯沙坦 100 mg/d [18]	24 h 蛋白尿下降 230 mg vs 253 mg；eGFR 下降 0.41 vs 0.76 mL/min/1.73 m^2；差异均无统计学意义；终点事件 8.6% vs 8.2% [18]	研究评估了安全性，但长期安全性和更高蛋白尿或更低 eGFR 人群的可推广性仍有限[18]	可作为标准治疗背景下的特定制剂比较证据，不能据此替代 KDIGO 疾病特异性治疗。
槐杞黄	前瞻性随机对照研究；45 例轻型 IgAN；12 周；蛋白尿 ≤2 g/d [26]	第 8、12 周蛋白尿和血尿改善；摘要未提供 eGFR 和长期肾脏结局 [26]	研究报告未观察到明显不良事件；停药后复发问题仍需研究 [26]	可视为短期替代终点信号，定位为探索性辅助干预。
雷公藤	重度蛋白尿患者队列；49 例；泼尼松、常规剂量和双倍剂量雷公藤方案比较[42]	双倍剂量组完全缓解率 87.5%，泼尼松组 69.2%，常规剂量组 0%；肾功能不全率和病理变化无显著差异[42]	该小样本队列未见严重不良事件；更广泛安全性资料提示胃肠、生殖、肝肾和血液等风险[29]	不宜作为一般替代治疗；仅可在严格风险评估、制剂质量控制和监测条件下作为探索性辅助方案。
益肾化湿颗粒	多中心随机对照研究；97 例；优化支持治疗基础上加用益肾化湿颗粒；8 周[17]	24 h 蛋白尿较对照多下降约 340 mg；基线蛋白尿 ＞1000 mg/d 者差异约 505 mg；eGFR 无显著组间差异[17]	8 周内不良事件率无显著差异；短期随访不能判断长期肾脏结局[17]	最符合“优化支持治疗上的附加干预”研究定位，但仍需长期、盲法和硬结局验证。

系统综述能够提高估计精度，但不能消除原始研究的偏倚和异质性。以非免疫抑制治疗为主题的 Cochrane 综述纳入的研究范围并不限于中医药，其总样本量不能直接作为中医药证据量；当不同制剂、对照和结局被合并时，合并效应也不等同于某一具体制剂的临床获益[5]。蛋白尿下降可作为 IgAN 试验中的合理替代终点，但单项短期研究不能证明肾衰竭风险下降，尤其不能替代对慢性 eGFR 斜率和长期肾脏生存的评价[4] [28]。

安全性证据同样不足。雷公藤及相关制剂存在肝肾毒性、生殖和血液系统毒性风险，草药与其他药物的相互作用资料也不完整。研究中未报告严重不良事件，不能等同于长期安全性已被证实；儿童、妊娠、高龄和严重肾功能减退患者也不能直接外推普通成人研究结果[24] [25] [29]-[31]。临床使用应明确产品来源、成分、剂量和疗程，记录合并用药，并监测肾功能、肝功能、血常规、电解质及与产品风险相关的指标。

中医理论部分常以“本虚标实”、肺脾肾相关和分期辨治解释 IgAN 的临床表现，证候研究则尝试把症状、病理和预后联系起来[20] [32]-[41]。这些内容可以帮助提出干预对象和分层假说，但证候分布、病名对应和现代病理分型并非同一分类体系，不能将理论一致性直接作为疗效或机制已被证实的依据。

临床研究中，黄葵、雷公藤、槐杞黄及辨证复方的结果各有差异；有的研究为中药与 ACEI 或 ARB 联用，有的研究采用活性药物对照，还有研究为小样本或非随机设计[18] [22] [23] [26] [42] [43]。这些研究可以提示值得进一步验证的方案，但不能在不区分制剂、剂量和对照的情况下合并为单一“中医药疗效”。

联合现代治疗的研究尤其需要明确增量效应。若两组均接受相同的 RAAS 阻断、SGLT2 抑制剂或其

他基础治疗，组间差异才更接近中医药的附加效应；若背景治疗随医生选择而变化，则结果可能同时反映适应证、疾病严重程度和治疗选择偏倚。研究还应报告依从性、救援治疗、失访和不良事件，避免用“总有效率”代替预先定义的临床结局。

证候、病理和预后之间的研究为精准分层提供了可能方向，但目前尚不能据此确定优势人群。证候要素与病理分型、蛋白尿、eGFR 或免疫标志物之间的关联，需要在独立队列和前瞻性试验中重复验证；否则，分期辨治只能作为临床假说，不能替代随机化比较[34]-[37]。

3.3. 中医药机制证据

机制研究提出了中医药可能影响黏膜免疫、异常 IgA 产生、免疫复合物及系膜沉积、补体激活、炎症信号、氧化应激、足细胞和肾小球滤过屏障、肾小管间质损伤及纤维化等假说[3] [44]-[54]。这些研究有助于提出可检验的生物学问题，但证据层级必须分开解释：人体干预或关联研究可以提供临床相关线索，动物和细胞实验主要说明潜在通路，网络药理学、分子对接和多组学研究则主要用于生成假说。

计算预测或通路富集不能证明患者体内存在有效暴露、直接靶点作用或因果疗效；动物模型中的通路变化也不能直接等同于患者获得长期肾脏获益[54]-[57]。因此，机制证据的合理结论应是“提示可能的作用路径”，而不是“证实治疗机制”。后续研究需要把药代暴露、患者生物样本、病理或生物标志物与临床终点联系起来，检验机制变化是否介导可重复的临床获益(见图 2)。



Figure 2. Evidence layers and interpretation boundaries for traditional Chinese medicine interventions in IgA nephropathy
图 2. 中医药干预 IgA 肾病的证据层级与解释边界

证据整合还应区分“研究对象”与“治疗类别”。一项具体制剂的结果不能外推到所有复方、单味药或中西医结合方案；动物模型中的药物剂量和给药途径也不能直接换算为患者用药。对于雷公藤等具

有明确毒性风险的药物，临床定位必须同时考虑疗效信号、适用人群、监测条件和替代治疗选择[24] [25] [29] [42]。

本文的临床判断具有明确边界。第一，中医药可能减少部分患者的蛋白尿或症状负担，但该判断主要来自异质性研究，不能表述为已证明改善长期肾脏生存。第二，机制研究可以解释为什么某些方案值得继续研究，但不能绕过人体疗效和安全性验证。第三，临床应用不是单纯选择“有效”或“无效”，而是要在标准治疗、患者风险、制剂质量、相互作用和监测可行性之间作出共同决策。

中医药的实施还涉及质量标志物、批次一致性和药物相互作用。产品质量、有效成分和暴露水平的差异，可能使同名制剂在不同研究中产生不同结果；即使某一研究观察到蛋白尿改善，也应确认结果是否与可重复的质量控制和可接受的风险监测相匹配[30] [58]。因此，治疗定位必须同时包含疗效不确定性和实施条件，而不能只写成“具有应用前景”。

4. 讨论

4.1. 中医药的临床定位

综合现有证据，中医药更适合被研究为优化标准治疗基础上的潜在辅助或探索性干预。其可能适用于病情相对稳定、规范治疗后仍存在残余蛋白尿或症状负担、能够接受规律监测且经过共同决策的患者。该定位不等同于疗效已经确立，也不支持用中医药替代 ACEI 或 ARB、SGLT2 抑制剂、靶向释放布地奈德、适宜患者的免疫抑制治疗或其他具有明确适应证的疾病特异性治疗[1] [2] [5] [17] [18] [24] [25]。

临床决策应先完成肾活检诊断和现代风险分层，确认基础治疗充分，再讨论中医药的可能增量价值。对于制剂来源不清、成分和批次不稳定、缺乏安全性监测或存在潜在相互作用的方案，不宜仅依据蛋白尿短期变化作出长期治疗承诺。临床记录应同时保留肾功能、蛋白尿、药物暴露、不良事件和患者报告结局，以便区分症状改善、替代终点变化与真正的肾脏获益。

研究报告还应完整描述干预措施。中药复方研究至少需要说明药材基原、炮制、处方组成、质量控制、批次、剂量、给药频次、疗程和依从性；随机试验应报告分配、盲法、失访和不良事件；系统综述应说明检索、筛选、偏倚评价和合并原则[59]-[63]。只有在这些信息充分时，重复研究和跨研究比较才具有可行性。

未来研究还应预先定义真正具有临床意义的目标人群和结局。可将蛋白尿作为早期疗效指标，但应同时设定慢性 eGFR 斜率、持续性 eGFR 下降或肾衰竭复合结局，并延长随访以观察效应是否持续。研究应说明患者是否接受指南一致的基础治疗，区分附加治疗与替代治疗，采用患者报告结局补充实验室指标，并建立主动的肝肾、生殖、血液和药物相互作用监测。

4.2. 证据局限与未来研究

当前证据的主要局限包括制剂和干预方案缺乏标准化，现代背景治疗不一致，随机化、盲法和分配隐藏报告不足，随访时间较短，以及对总有效率和蛋白尿等替代终点依赖较多。机制研究与临床研究之间也缺乏统一的暴露、标志物和结局链条。这些问题会降低估计的确定性，并限制研究结果向不同人群、不同产品和长期肾脏结局的外推。

未来应在优化标准治疗背景下开展预注册、多中心、随机、双盲、安慰剂对照的附加治疗试验，明确制剂基原、炮制、质量控制、剂量和疗程，并预先规定蛋白尿、慢性 eGFR 斜率、持续性 eGFR 下降、肾衰竭复合结局、患者报告结局和安全性指标。CONSORT、SPIRIT、PRISMA、TIDieR 及中药复方报告规范可用于改进试验、方案、系统综述和干预描述的透明度[59]-[63]。研究设计还应使用目标试验模拟等方法减少观察性研究的混杂，但其结果仍需与随机试验相互验证[64] [65]。

5. 结论

KDIGO 2025 框架下，中医药研究应回答的是其在规范治疗基础上能否提供独立、可重复且具有临床意义的增量获益，而不是仅证明存在潜在生物学通路。现有证据提示部分制剂或联合方案可能改善短期蛋白尿，但受制剂异质性、基础治疗不一致、研究质量有限、随访不足和安全性资料不完整影响，尚不能据此推断长期 eGFR 保持或肾衰竭风险下降。中医药目前宜定位为潜在辅助或探索性干预，未来价值取决于标准化制剂和长期随机附加治疗试验的验证。

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