IgA Nephritis: Known threat, unknown plan for older transplants

Written by The Life Science Feed Editorial Team · Published 29 July 2026 · Edited by Mara Voss

IgA nephritis, a leading cause of primary glomerulonephritis, frequently recurs after kidney transplantation, posing a substantial threat to graft survival. While treatment strategies exist for younger populations, the evidence base for older, post-transplant patients remains remarkably thin. This demographic faces unique challenges, including polypharmacy, altered immune responses, and increased comorbidity burden, all of which complicate therapeutic decisions.

The lack of dedicated research means clinicians often extrapolate data from younger cohorts or other kidney diseases, a practice fraught with uncertainty. This approach may lead to suboptimal outcomes, given the distinct physiological and immunological profiles of older transplant recipients. A clear need exists for targeted investigations to inform evidence-based management in this vulnerable group.

KEY TAKEAWAYS

- The Pivot: Existing IgA nephritis trials consistently underrepresent or exclude older, post-transplant patients, creating a critical evidence void.
- The Data: No specific hazard ratios or p-values are available for IgA nephritis recurrence or graft loss in older transplant recipients due to insufficient dedicated research.
- The Action: Clinicians must acknowledge the absence of robust data for older IgA nephritis transplant patients and advocate for their inclusion in future trials.

IgA nephritis (IgAN) stands as the most common primary glomerulonephritis globally, frequently progressing to end-stage kidney disease (ESKD). For patients undergoing kidney transplantation, IgAN recurrence in the allograft is a well-documented and concerning complication, occurring in approximately 30-60% of recipients within 10 years post-transplant. This recurrence significantly impacts long-term graft survival, often leading to graft dysfunction and eventual loss. The pathophysiology involves the deposition of aberrantly glycosylated IgA1 in the mesangium, triggering an inflammatory cascade. In the transplant setting, this process can be exacerbated by donor-specific antibodies or other immune dysregulation.

The challenge intensifies when considering older patients, typically defined as those over 65 years of age, who receive kidney transplants. This demographic represents a growing proportion of transplant recipients, driven by an aging population and expanded donor criteria. But, despite their increasing numbers, older patients are consistently underrepresented or entirely excluded from clinical trials investigating treatments for recurrent IgAN. This creates a

substantial knowledge gap, forcing clinicians to navigate complex treatment decisions without the guidance of robust, age-specific evidence.

The Uncharted Territory of Older Patients

Most clinical trials for IgAN, whether in native kidneys or post-transplant, impose strict age cut-offs, often limiting enrollment to individuals under 65 or even 70 years. This exclusion is typically justified by concerns about comorbidities, polypharmacy, and the potential for increased adverse events in older participants. But, this practice inadvertently marginalizes a significant patient population. For instance, a review of major IgAN trials over the past decade reveals that the mean age of participants rarely exceeds 50 years, with very few studies reporting subgroup analyses for older adults. This means that the efficacy and safety data generated from these trials, while valuable for younger cohorts, cannot be reliably extrapolated to older recipients.

The immunological milieu of an older transplant recipient differs considerably from that of a younger individual. Immunosenescence, the age-related decline in immune function, affects both innate and adaptive immunity. This can lead to altered responses to immunosuppressive medications, potentially increasing the risk of infection or malignancy, while simultaneously impacting the effectiveness of therapies aimed at modulating IgAN recurrence. Older patients also frequently present with a higher burden of cardiovascular disease, diabetes, and other chronic conditions, which can complicate the management of IgAN and its treatments. These factors are rarely accounted for in trial designs focused on younger, healthier populations.

Therapeutic Dilemmas and Data Deficiencies

Current treatment approaches for recurrent IgAN post-transplant often mirror those used for native kidney IgAN, including corticosteroids, mycophenolate mofetil, and calcineurin inhibitors. But, the optimal dosing, duration, and combination of these agents in older transplant recipients with recurrent IgAN remain largely undefined. For example, corticosteroids, a cornerstone of IgAN therapy, carry a higher risk of adverse effects in older patients, including bone demineralization, glucose intolerance, and increased susceptibility to infections. The risk-benefit profile shifts considerably with age, yet specific guidelines or trial data to inform this balance are absent.

Consider the use of rituximab, a B-cell depleting agent, which has shown some promise in selected cases of recurrent IgAN. While data in younger patients suggest potential benefits, its use in older, immunosuppressed transplant recipients raises concerns about profound B-cell depletion and subsequent infection risk. Without dedicated studies, clinicians must weigh these theoretical risks against potential benefits based on limited anecdotal evidence or extrapolation from non-transplant settings. This is not evidence-based medicine; it is an educated guess.

The lack of data extends beyond specific drug efficacy to fundamental aspects of disease management. What is the optimal biopsy strategy for older patients with suspected IgAN recurrence? Are the histological criteria for diagnosis and prognosis the same as in younger individuals? How should proteinuria thresholds for intervention be adjusted in the context of age-related changes in renal physiology and existing comorbidities? These are not trivial questions; they directly impact patient care and long-term graft outcomes. The Oxford Handbook of Nephrology and Hypertension provides a comprehensive overview of general renal disease management, but even such authoritative texts cannot fill the void of specific trial data for this niche population.

Designing for Inclusion, Not Exclusion

The prevailing practice of excluding older patients from clinical trials is a significant limitation that perpetuates the evidence gap. Future trial designs must actively seek to include older individuals, perhaps through adaptive trial designs or by establishing dedicated geriatric cohorts. This would necessitate careful consideration of endpoints relevant to older patients, such as quality of life, functional status, and treatment tolerability, in addition to traditional graft survival metrics. Stratification by age and comorbidity burden could also provide valuable insights into differential treatment responses.

But, designing such trials presents its own set of challenges. Older patients often have multiple comorbidities, which can confound results and increase variability. Polypharmacy is common, leading to potential drug-drug interactions that complicate safety assessments. Recruitment can also be difficult, as older patients may be less willing or able to participate in demanding clinical protocols. These are not insurmountable obstacles, but they require thoughtful planning and resource allocation. Collaborative efforts across multiple transplant centers could help achieve adequate sample sizes for meaningful analyses in this population.

The absence of data for older, post-transplant IgAN patients is not merely an academic oversight; it has direct clinical consequences. It means that a growing segment of the transplant population receives care based on assumptions rather than evidence. This situation is particularly concerning given the increasing life expectancy of transplant recipients and the rising age of both donors and recipients. As the transplant community strives for personalized medicine, ignoring an entire demographic due to age-related exclusions is a disservice to both patients and the principles of evidence-based practice.

The Path Forward: A Call for Dedicated Research

The imperative is clear: more research is needed, specifically designed for older, post-transplant patients with IgAN. This includes observational studies to better characterize the natural history of recurrent IgAN in this population, as well as interventional trials to evaluate the efficacy and safety of various therapeutic strategies. These studies should incorporate geriatric assessment tools to capture relevant outcomes beyond graft function, such as frailty, cognitive function, and quality of life. The goal must be to generate data that directly informs clinical decisions, moving beyond reliance on extrapolation.

Without such dedicated efforts, clinicians will continue to operate in a data desert, making difficult choices with limited guidance. The transplant community has a responsibility to ensure that all patient groups, regardless of age, benefit from the advancements in medical science. Until then, the management of recurrent IgAN in older transplant recipients remains an area of significant unmet need and clinical uncertainty.

> **CLINICAL IMPLICATIONS**
>
> The persistent exclusion of older kidney transplant recipients from IgA nephritis trials is a glaring omission. Clinicians are left to manage recurrent IgAN in this vulnerable population using protocols derived from younger, healthier cohorts, a practice that ignores the fundamental physiological and immunological differences that come with age. This isn't just suboptimal; it's a disservice to patients who increasingly comprise a significant portion of transplant recipients.
>
> The industry, particularly pharmaceutical companies developing new immunomodulatory agents, must recognize this unmet need. Designing trials that accommodate the complexities of older patients, including

> their comorbidities and polypharmacy, is not merely an ethical consideration; it represents a significant market opportunity. The current approach of broad exclusion is simply lazy science, failing to provide the comprehensive data required for real-world clinical practice.
>
> For general practitioners and specialists alike, the message is to acknowledge the limitations of current evidence. When faced with an older patient experiencing recurrent IgAN post-transplant, recognize that much of what we 'know' is extrapolated. This necessitates a highly individualized approach, careful monitoring for adverse effects, and a frank discussion with patients about the uncertainties inherent in their treatment plan. We cannot pretend the evidence exists when it demonstrably does not.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Healio. More research needed in older, posttransplant patients with IgA nephritis. Accessed Jul 2026. https://www.healio.com/news/nephrology/20260713/more-research-needed-in-older-posttransplant-patients-with-iga-nephritis

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com