



Monoclonal Gammopathy of Renal Significance: Clinical Insights and Therapeutic Advances

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ABSTRACT

Monoclonal gammopathy of renal significance (MGRS) describes a group of kidney disorders driven by nephrotoxic monoclonal immunoglobulins arising from small, indolent clones of B cells or plasma cells. Although these clones fall short of the diagnostic thresholds used for hematological malignancy, the monoclonal protein they secrete can injure the kidney directly or through tissue deposition. The renal compartment affected—glomerulus, tubule, interstitium, or vasculature—and the resulting clinical picture depend largely on the physicochemical behavior of the paraprotein, and untreated disease tends to progress to chronic kidney failure.

Diagnostic precision in MGRS has improved considerably with refinements in renal biopsy interpretation and wider use of immunofluorescence, electron microscopy, and mass spectrometry-based proteomics. Linking hematological work-up with renal diagnostics now permits earlier disease recognition and more precisely targeted intervention. Management has moved away from nonspecific immunosuppression toward clone-directed regimens—proteasome inhibitors, monoclonal antibodies, and immunomodulatory agents—chosen to suppress the underlying clone while sparing renal function.

Because no single specialty can manage MGRS alone, close cooperation between nephrologists, hematologists, and renal pathologists has become the standard of care, and early clone-directed treatment is associated with better renal and survival outcomes. Open questions remain around biomarker development, standardized diagnostic pathways, and minimization of treatment toxicity; addressing these will require sustained multidisciplinary research. This review summarizes current understanding of MGRS pathophysiology, diagnosis, and treatment, and outlines the gaps that future work should address.

Keywords: Amyloidosis, Diagnostic advancements, Light chain deposition disease, Monoclonal gammopathy of renal significance, Monoclonal immunoglobulin deposition disease, Plasma cell dyscrasia, Renal pathology, Targeted therapy.

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INTRODUCTION

The term monoclonal gammopathy of renal significance (MGRS) was coined in 2012 by the International Kidney and Monoclonal Gammopathy Research Group (IKMG) to capture a specific category of kidney disease.¹ Two features define MGRS: the disease is driven by a nephrotoxic monoclonal immunoglobulin, and that immunoglobulin is secreted by a B-cell or plasma cell clone too small to meet criteria for multiple myeloma or malignant lymphoma.² This review traces how the definition and terminology of MGRS have evolved, summarizes recent diagnostic and therapeutic progress, and considers what these advances mean for everyday clinical practice.

The International Kidney and Monoclonal Gammopathy Research Group revisited the classification of MGRS-related renal lesions in 2017 and sharpened the definition further.^{2,3}

Why Did the Definition Need Revision?

The original concept of MGRS cast a wide net, covering any small B-cell clone capable

of producing a harmful monoclonal protein. That breadth created ambiguity: it was unclear whether smoldering multiple myeloma (SMM) or smoldering Waldenström macroglobulinemia (SWM) belonged under the MGRS umbrella, and a similar question arose for indolent chronic lymphocytic leukemia (CLL) or low-grade lymphomas that, although technically malignant, do not yet warrant treatment.⁴

The revised definition narrows MGRS to B-cell and plasma-cell disorders that produce a nephrotoxic monoclonal immunoglobulin but do not themselves require immediate oncological treatment. SMM, SWM, monoclonal B-cell lymphocytosis (MBL), and indolent lymphomas causing renal injury are all captured by this updated definition, which explicitly excludes any requirement for overt malignancy; once a clone progresses to frank malignancy, management follows disease-specific protocols rather than the MGRS framework.⁵

With this clarified definition as a foundation, the discussion can now turn to

the range of renal histopathological patterns seen in MGRS and what they mean for clinical care.

THE SPECTRUM OF RENAL HISTOPATHOLOGY IN MGRS

Because of their size, intact monoclonal immunoglobulins do not cross the glomerular basement membrane; free light chains, being considerably smaller, pass through the filter and are normally reclaimed and degraded by proximal tubular cells. Nephrotoxicity in MGRS arises through several overlapping mechanisms—tissue deposition with direct cellular interaction, intratubular precipitation, and activation of complement and inflammatory cytokine pathways. The paraprotein deposited in the kidney may be an intact immunoglobulin, an isolated light or heavy chain, a light-heavy chain combination, or a fragment of any of these. Any of the four renal compartments—glomerulus, tubule, interstitium, or vessel—may be involved, alone or together.⁶ Which compartment is affected, and how severely, depends largely on the structural and physicochemical properties of the specific paraprotein, properties that can render it nephrotoxic even at low circulating concentrations.^{7,8} Recognizing this histopathological spectrum is central to interpreting the clinical significance of MGRS and to choosing an appropriate management strategy.⁹

Table 1 summarizes the classification and salient clinical, immunofluorescence, ultrastructural, and extrarenal features of the principal MGRS-associated lesions.^{9–13}

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Table 1: Monoclonal gammopathy of renal significance (MGRS) classification

Category	Kidney symptoms	Immunofluorescence (Ig type)	Ultrastructural features	Extrarenal manifestations
AL Amyloidosis	Proteinuria, nephrotic syndrome (NS), CKD; occasionally hypertension and hematuria	Light chain (λ predominant)	Unbranched fibrils, 7–14 nm	Heart, liver, nerves
AH Amyloidosis	Same as AL	Heavy chain ($\gamma 1$, $\gamma 4$, or α)	Same as AL	Same as AL
AHL Amyloidosis	Same as AL	Light + Heavy ($\gamma + \lambda$ or $\alpha + \kappa$)	Same as AL	Same as AL
ITGN / GOMMID	Proteinuria, NS, CKD, microhematuria, hypertension, AKI, nephritic syndrome	Monotypic IgG (IgG1–3), κ or λ ; C3, C4, C1q deposits	Microtubules (10–60 nm), hollow	Rare: nerves, skin
Type I Cryoglobulinemic GN	Proteinuria, NS, CKD, microhematuria, hypertension, AKI, nephritic syndrome	Monotypic IgG/IgM/IgA (κ or λ); C3, C4, C1q deposits	Microtubules (10–90 nm), crystals possible	Skin, nerves, joints
Light Chain Fanconi Syndrome	Proximal tubular dysfunction, gradual CKD progression	Mostly κ (Vk1 or Vk3)	Rhomboid crystals in lysosomes	Osteomalacia, bone disease
Crystal-Storing Histiocytosis	Proximal tubulopathy, CKD	Predominantly κ (Vk1 or Vk3)	Needle-like crystals in histiocytes	Multi-organ: liver, lungs, cornea
MIDD (LCDD / HCDD / LHCD)	Proteinuria, NS, CKD, microhematuria, hypertension	Linear Ig deposits (LCDD: LC, HCDD: HC, LHCD: LC+HC)	Amorphous deposits in GBM, TBM, mesangium	Heart, liver, lungs
PGNMID	Proteinuria, NS, CKD, microhematuria, hypertension	Monotypic IgG, usually IgG3	Non-organized granular deposits	None
C3 Glomerulopathy with MG	Proteinuria, NS, CKD, microhematuria, hypertension	Sparse/absent Ig; prominent C3	Intramembranous & mesangial dense deposits	None

Table 2: Summary of methods for detecting monoclonal free light chains (FLCs)

Method	Type	Detection limit (sensitivity)	Advantages	Disadvantages
Serum protein electrophoresis (SPE)	Semiquantitative	500–2000 mg/L	Affordable and simple to perform	Limited sensitivity for low levels of M-proteins, especially FLCs.
Urine protein electrophoresis (UPE)	Semi-quantitative	20–50 mg/L	Inexpensive and straightforward	Detects FLCs only when tubular reabsorption is saturated; requires 24-hour urine collection; interpretation can be subjective; challenging with concentrated urine or high protein levels.
Serum Immunofixation Electrophoresis (IFE)	Qualitative	150–500 mg/L	About 10 times more sensitive than serum EP	Detects urinary FLCs only once reabsorption is overwhelmed; needs 24-hour urine collection.
Urine Immunofixation Electrophoresis (IFE)	Qualitative	20–50 mg/L	Useful as a prognostic tool and for monitoring treatment effectiveness	Requires 24-hour urine collection; similar limitations to serum IFE.
Serum free light chain assay (sFLC)	Quantitative	κ : 1.5 mg/L; λ : 3 mg/L	Precise κ/λ measurement and ratio; helpful for prognosis and treatment monitoring	More expensive; inter-assay variability; needs further refinement for certain diseases.

When to Suspect MGRS

A nonmalignant or premalignant monoclonal gammopathy is found incidentally in a substantial proportion of patients investigated for unexplained renal impairment or proteinuria, particularly among older adults.

Clinicians should consider MGRS whenever renal disease coexists with a detectable M-protein, especially when conventional cardiovascular risk factors—diabetes, hypertension, atherosclerosis—are either absent or already well controlled. The same suspicion should extend to patients with C3 glomerulopathy or thrombotic microangiopathy (TMA), both of which show a recognized association with M-protein-driven kidney disease, again more so in older patients. MGRS is most often diagnosed

beyond age 50, though it is not confined to this group.¹⁴

Monoclonal Protein Testing

Because the underlying clone in MGRS is small, circulating M-protein levels are typically low. Serum protein electrophoresis (SPE)—with a detection floor of roughly 500–2000 mg/L—frequently misses these low-level paraproteins, particularly free light chains (FLCs), which clear from the circulation faster than intact immunoglobulins. Serum immunofixation electrophoresis (IFE) improves sensitivity roughly tenfold over SPE, but reliably identifying the M-protein usually still requires urine IFE and/or a serum free light chain assay.^{9,15–17} Table 2 compares the sensitivity, advantages, and limitations

of the principal methods used to detect monoclonal free light chains.

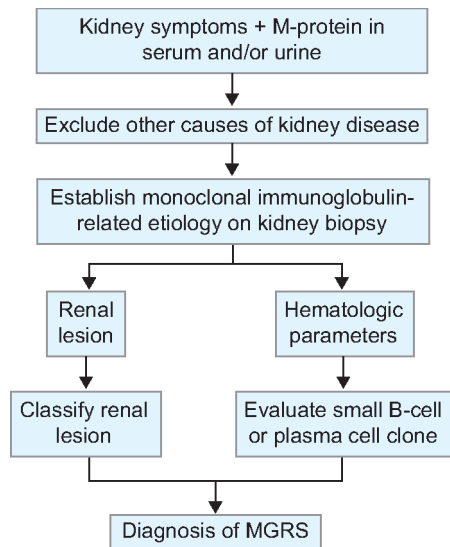
Kidney Biopsy and Bone Marrow Evaluation in MGRS Diagnosis

A kidney biopsy is the pivotal investigation in MGRS, distinguishing an incidental M-protein from one that is actually driving the renal lesion. A full assessment—immunofluorescence (IF), immunohistochemistry (IHC), and electron microscopy (EM)—is needed to characterize deposit composition and ultrastructure. EM is especially valuable for fibrillary glomerulonephritis (FGN), immunotactoid glomerulopathy (ITG), type 1 crystalline glomerulopathy, and crystalline light-chain proximal tubulopathy (LCPT). When AL amyloidosis is suspected, however, a surrogate

Table 3: Special stains used on renal biopsy tissue in MGRS

Disease	PAS	Silver stain	Masson's trichrome	Congo red
Amyloid	–	–	Blue	+++
ITG/FGN	+++	–	Blue	–
FN	–	–	Red	–
DN	+++	+	Blue	–
MIDD	–	–	Blue	–
INS	+++	+	Blue	–
CG	–	–	Blue	–

PAS, periodic acid–Schiff stain; ITGN, immunotactoid glomerulopathy; FGN, fibrillary glomerulonephritis; FN, fibronectin glomerulopathy; DN, diabetic nephropathy; MIDD, monoclonal immunoglobulin deposition disease; INS, idiopathic nodular sclerosis; CG, crystalline glomerulopathy


Fig. 1: Diagnostic algorithm for MGRS

tissue sample such as abdominal fat may sometimes substitute for renal biopsy if there is clinical evidence of renal involvement.¹⁴

Certain dense or unusual deposits require more specialized methods—immunogold EM or proteomic analysis by laser microdissection coupled with mass spectrometry (LMD/MS). LMD/MS is now the reference standard for amyloid typing and is also useful in other MGRS subtypes, though it typically requires referral to a specialized laboratory and is reserved for diagnostically ambiguous cases.^{18,19}

Identifying the causative B-cell or plasma-cell clone calls for a thorough hematological evaluation that excludes overt multiple myeloma or Waldenström macroglobulinemia. Bone marrow aspirate and biopsy in MGRS usually show only a modest, morphologically unremarkable increase in plasma cells or B cells (under 10%). A Congo red stain of the marrow can flag amyloidosis, which is detectable there in roughly 60% of AL amyloidosis cases, while immunohistochemistry and flow cytometry confirm clonality and correlate it with the circulating M-protein.²

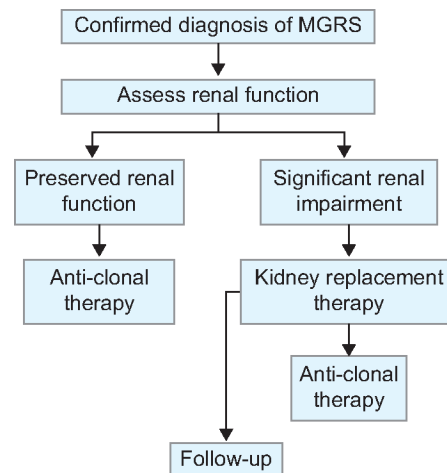

Fig. 2: Treatment algorithm for MGRS

Table 3 lists the special stains used on renal biopsy tissue and the patterns they reveal across the major MGRS-related lesions, and Figure 1 sets out a diagnostic algorithm that brings these elements together.

TREATMENT AND ADVANCES IN THE FIELD OF MGRS

Management of MGRS targets the underlying B-cell or plasma-cell clone. Historically, clinicians were reluctant to treat MGRS aggressively, worried about toxicity—particularly the risk of secondary malignancy with alkylating agents—at a time when the condition was generally regarded as indolent. Autologous peripheral blood stem cell transplantation has since proven a workable option for B-cell clones, and ongoing monitoring remains essential to catch complications such as thrombosis or infection, especially when nephrotic-range proteinuria is present.²⁰ Figure 2 outlines the basic treatment strategy.

For patients with CKD stages 1–3, early chemotherapy aimed at suppressing monoclonal immunoglobulin production and achieving a deep hematological response is advised.²¹ Autologous stem cell transplantation (ASCT) can deepen

and prolong both the hematological and renal response. Conservative measures—bicarbonate, phosphate binders, and vitamin D—help offset CKD-related mineral and bone disease, and renin–angiotensin–aldosterone blockade (ACE inhibitors or ARBs) is appropriate for hypertension. Dialysis becomes necessary once patients reach end-stage renal disease (ESRD), with kidney transplantation the preferred long-term option, although recurrent nephropathy after transplant remains common, particularly when the underlying clone was not adequately controlled beforehand. While no MGRS-specific trial has yet proven a survival benefit, large trials of SGLT2 inhibitors and finerenone have shown improved renal outcomes and reduced mortality in CKD more broadly, and these agents are reasonable to consider in MGRS as well.²²

In CKD stage 4 or ESRD, chemotherapy is generally reserved for patients who remain transplant candidates or who have significant extrarenal disease—cardiac, hepatic, or pulmonary. A complete hematological response before transplantation is important to limit the risk of MGRS recurrence and graft loss in the new kidney; ASCT may be used pre-transplant to help achieve this, and treating extrarenal disease can separately improve organ-specific outcomes.^{7,23}

Plasma Cell Dyscrasia with IgG, IgA, or LC Only

When a non-IgM MGUS clone secretes only IgG, IgA, or light chains, treatment is directed at clone eradication to protect renal function. Bortezomib, a proteasome inhibitor that is cleared largely independent of the kidney, is the workhorse agent, usually paired with dexamethasone. It produces rapid reduction in tumor burden and improves renal function in multiple myeloma patients with renal impairment, and in dialysis-dependent myeloma patients, bortezomib-based induction has outperformed conventional chemotherapy in lowering transplant-related mortality. The same regimen—often combined with melphalan-conditioned ASCT—produces high complete and very good partial response rates in AL amyloidosis; giving bortezomib both before and after ASCT can help offset the impact of renal failure on outcomes.²⁴

Eligibility for ASCT matters as much as drug choice. Patients under 70 with adequate cardiopulmonary reserve, stable renal disease, and good performance status are generally suitable candidates; ASCT remains feasible even on dialysis, albeit with a higher risk of transplant-related death, and is best avoided in patients with active infection or otherwise unmet eligibility

Table 4: Treatment recommendations and transplant considerations

MGRS Entity	Treatment recommendation	Transplant notes
MIDD	CKD I–III: Bortezomib-based therapy ± ASCT if eligible; CKD IV–V: same, with continued therapy if not transplant eligible	Success depends on effective hematologic treatment before transplant
PGNMID	CKD I–II, stable: symptom management; progressive CKD or CKD III–V: chemotherapy ± ASCT if eligible	High recurrence risk without treatment; histologic monitoring crucial
ITG	Treat CLL-associated cases with bendamustine + rituximab; non-CLL: bortezomib-based regimens	Outcome depends on underlying hematologic response
Type 1 Cryoglobulinemic GN	Plasma cell clone: myeloma-directed therapy ± ASCT; LPL clone: WM-like therapy (rituximab-based)	Transplant success relies on pre-transplant therapy and hematologic response
Type 2 Cryoglobulinemic GN	HCV+: antivirals ± immunosuppression; rapid progression: add plasma exchange	Viral management key; monitor vasculitis pre/post-transplant
LCPT with Fibrillary Structures	CKD I–III: chemotherapy (bortezomib ± ASCT); CKD IV–V: similar, with symptom focus if transplant ineligible	High recurrence risk without hematologic control; pre-transplant therapy is critical

criteria. Those who are not ASCT candidates typically receive six to eight cycles of bortezomib with dexamethasone and cyclophosphamide, or bortezomib with melphalan-prednisone. Thalidomide and lenalidomide are reasonable immunomodulatory alternatives, with lenalidomide generally favored on efficacy grounds.²⁵

B-cell Clone with IgM M-protein

IgM MGUS-driven MGRS is uncommon, so the supporting evidence base is correspondingly thin. Where the clone is IgM-secreting and B-cell in origin, rituximab—typically combined with dexamethasone plus either cyclophosphamide or bendamustine—is the preferred approach. Rituximab needs no dose adjustment for renal impairment; cyclophosphamide elimination is affected by renal function, though recommended dose adjustments vary across the literature, and bendamustine appears reasonably safe in moderate renal impairment but carries more toxicity risk as kidney function falls further. ASCT remains an option for patients likely to achieve a substantial hematological response.²⁶

Transplant in MGRS

Whether and when to transplant a kidney in MGRS remains unsettled. Recurrence risk is higher than in the general transplant population, and there is no consensus on optimal timing. Nonetheless, kidney transplantation can be appropriate for MGRS patients reaching ESRD, since effective hematological treatment improves both renal prognosis and overall survival; patients who respond well to rescue therapy tend to have correspondingly better graft survival, which is why transplantation is generally reserved for those who have already achieved a good hematological response, even though some recurrence risk persists regardless.^{5,14,27–29}

Outcomes after transplant differ by the structural type of the deposit. MGRS entities with organized Ig deposits—

fibrillary, microtubular, or crystalline—have outcomes that hinge on how well, and how promptly, the clone was treated before transplant. Nonorganized deposits, as in C3 glomerulopathy or TMA, carry a particularly high risk of early recurrence if the underlying clone is left untreated; a Mayo Clinic series reported an 89% recurrence rate without prior hematologic control, vs 30% when control was achieved.³⁰

Treatment of PGNMID should follow the suspected or confirmed clone: regimens built around cyclophosphamide, bortezomib, and dexamethasone suit a plasma-cell clone, while rituximab-based therapy is preferred for a B-cell clone; when no clone can be identified, empirical therapy is chosen based on the most likely cell of origin.

Table 4 summarizes treatment recommendations and transplant considerations across the major MGRS entities.

NOVEL THERAPEUTIC AGENTS AND DRUG CLASSES

Clone-directed therapy in MGRS has broadened substantially in recent years, with monoclonal antibodies, proteasome inhibitors, and complement blockers reshaping outcomes.

Monoclonal antibodies: Daratumumab, an anti-CD38 antibody, has become central to treating plasma-cell-mediated MGRS, AL amyloidosis in particular. In the phase III ANDROMEDA trial, adding daratumumab to CyBorD (cyclophosphamide, bortezomib, dexamethasone) nearly tripled the complete hematological response rate compared with CyBorD alone (53% vs 18%) and substantially improved the renal response rate (53% vs 24%).³¹ Daratumumab has also shown encouraging activity in LCDD and in PGNMID without an identifiable clone,³² while rituximab remains the standard for IgM-associated and other B-cell-driven MGRS.³³

Proteasome inhibitors: Bortezomib-based regimens remain first-line for plasma-cell MGRS such as AL amyloidosis and LCDD, valued for rapid tumor-cell lysis and renal recovery.³⁴ Carfilzomib and oral ixazomib are increasingly used in relapsed or refractory disease.

Immunomodulatory drugs (IMiDs): Lenalidomide and pomalidomide have a role in refractory disease but are used cautiously in amyloidosis because of toxicity concerns; their evidence base is stronger in nonamyloid lesions.³⁴

BCL-2 inhibitors: Roughly half of AL amyloidosis cases carry the t(11;14) translocation, making venetoclax—a BCL-2 inhibitor—a rational option; deep hematological responses have been reported in relapsed MGRS with this translocation.³⁵

Complement inhibitors: The C5 blocker eculizumab has been used in MGRS-associated TMA and C3 glomerulopathy, achieving dialysis independence in over half of TMA patients in one cohort,³⁶ though clone-directed therapy is still considered essential alongside complement blockade in complement-mediated disease.³⁷

Key Clinical Trials in MGRS

1. ANDROMEDA (2020–2021): adding daratumumab to CyBorD produced superior hematological and renal responses in AL amyloidosis.³¹
2. Daratumumab in PGNMID (2021): an open-label Mayo Clinic phase II trial found that daratumumab monotherapy produced a renal response in every enrolled patient.³²
3. C3G and clone therapy study (2017): clone-directed therapy improved renal survival compared with immunosuppression alone in MGRS-associated C3 glomerulopathy.³⁷
4. Ongoing studies: trials of CAEL-101 (an anti-light-chain amyloid antibody), in AL amyloidosis, and of isatuximab, and subcutaneous daratumumab in non-amyloid MGRS lesions, are currently underway.³⁸

Table 5: Response to therapy in MGRS

Response category	Criteria
Complete response	Normal free light chain (FLC) ratio; negative serum and urine immunofixation
Very good partial response	Difference between involved and uninvolved FLC < 40 mg/L
Partial response	≥50% reduction in the difference between involved and uninvolved FLC
No response	No significant change in FLC levels

RESPONSE TO THERAPY

In AL amyloidosis, LCDD, and Fanconi syndrome, response is graded by free light chain (FLC) kinetics. A complete response requires a normalized FLC ratio together with negative serum and urine immunofixation. A very good partial response is defined as a difference between involved and uninvolved FLC of under 40 mg/L, and a partial response as a fall of more than 50% in that difference; no meaningful change in FLC levels is classed as no response (Table 5).

Where the causal protein is an intact immunoglobulin, the response criteria used in multiple myeloma apply instead. If no causative immunoglobulin can be measured at all, response is instead assessed by repeat bone marrow examination. Complete hematological remission should be achieved before transplantation wherever possible, since recurrence risk is substantial across all MGRS subtypes and graft loss can occur particularly quickly in PGNMID.³⁹ Post-transplant care therefore requires close surveillance of immunoglobulin parameters, with therapy resumed promptly if the clonal disorder shows signs of progression.

RESEARCH GAPS AND FUTURE DIRECTIONS

Despite growing recognition of MGRS as a distinct entity, several gaps in knowledge persist:

1. *Few disease-specific clinical trials:* Most current treatment strategies are extrapolated from trials conducted in multiple myeloma, AL amyloidosis, or indolent B-cell lymphoma rather than in MGRS itself. Randomized trials specifically addressing non-amyloid MGRS subtypes—PGNMID, LCPT, immunotactoid glomerulopathy—are essentially absent, which limits the field's ability to build subtype-specific, evidence-based treatment algorithms.
2. *Delayed diagnosis and under-recognition:* Diagnosis is commonly delayed because of low-level, subclinical M-protein that conventional serum electrophoresis fails to detect; limited awareness of

MGRS among general nephrologists and hematologists; and reluctance to biopsy patients labeled simply as having "monoclonal gammopathy of unknown significance." Because delayed treatment risks irreversible renal damage, earlier recognition is a priority.

3. *No validated biomarkers:* There is currently no validated, noninvasive biomarker that reliably distinguishes MGRS from a benign monoclonal gammopathy. Mass-spectrometry-based proteomics, complement-activation assays, and urinary monoclonal light-chain profiling are promising but remain investigational.
4. *Difficulty monitoring disease activity:* Monitoring is complicated by discordance between hematological and renal responses, by clones that cannot be quantified in the first place (as in PGNMID without a detectable serum clone), and by the lack of a renal response standard that applies uniformly across histological subtypes. Serum free light chains and M-protein levels, the current mainstays of monitoring, do not necessarily track ongoing kidney injury.
5. *High recurrence after kidney transplantation:* Even though transplantation is now considered feasible in carefully selected patients, recurrence remains common, especially when hematological remission was incomplete beforehand. How long clone suppression should be maintained before transplant, and what role maintenance therapy should play afterward, are both still undefined.
6. *Need for multidisciplinary care models:* MGRS care depends on coordinated input from nephrology, hematology, pathology, and transplant teams, yet integrated care pathways are far from universal, particularly in resource-limited settings—a gap that risks fragmented care and missed opportunities for early treatment.

LIMITATIONS

This review has certain limitations inherent to its narrative format. It draws on published trial and cohort data rather than a systematic

or meta-analytic synthesis, so the selection of studies discussed, while intended to be representative, is not exhaustive. Much of the therapeutic evidence cited is extrapolated from trials conducted in multiple myeloma or AL amyloidosis rather than from MGRS-specific randomized trials, which remain lacking for most non-amyloid subtypes. Treatment recommendations for individual MGRS entities are therefore largely consensus- and expert-opinion-based rather than derived from high-level evidence, and outcome data—particularly for transplant recurrence and long-term renal survival—come mainly from retrospective, single-center, or registry series that carry their own selection and reporting biases.

CONCLUSION

Monoclonal gammopathy of renal significance comprises a wide range of kidney disorders unified by their relationship to a monoclonal protein rather than by a single histological pattern. Progress in understanding its pathophysiology, refining its diagnosis, and individualizing its treatment has materially improved how these patients are managed, and the experience reviewed here underscores how much that progress depends on close collaboration between nephrology, hematology, and pathology.

Three points are worth emphasizing:

1. Early diagnosis limits the risk of irreversible kidney damage.
2. Treatment succeeds or fails largely on how effectively the underlying B-cell or plasma-cell clone is controlled.
3. Newer clone-directed agents—daratumumab, venetoclax, and complement blockers among them—offer real grounds for optimism, even though kidney transplantation in this setting still calls for caution given the persistent risk of disease recurrence.

Further progress will depend on continued, cross-disciplinary research into MGRS-specific biomarkers, standardized response criteria, and disease-specific trials, with the shared goal of improving outcomes for patients living with this condition.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This is a narrative review article based on previously published literature and does not involve original patient data, identifiable patient information, or new human or animal experimentation. Ethics committee approval and participant consent are therefore not applicable.

CLINICAL TRIAL REGISTRATION

Not applicable—this manuscript does not report a clinical trial.

AUTHOR CONTRIBUTIONS

HSM contributed to the conception and design of the review. AR performed the literature search and drafted the manuscript. MSB and LSP critically revised the manuscript for important intellectual content. HSM supervised the work and provided final approval of the version to be published. All authors read and approved the final manuscript.

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