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Clinical and Pathological Characteristics of Non-AL Amyloidosis MGRS: A Single-Center Experience Over 10 Years

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Abstract

Objective: Monoclonal gammopathy of renal significance (MGRS) is a heterogeneous and relatively recently defined disorder that encompasses many kidney and hematologic pathologies. MGRS remains a rare disease and there is a need for more literature regarding its treatment and outcomes. In this study, we share our center's experience with MGRS including incidence of different kidney pathologies, clone type, kidney and hematologic response, and progression-free survival.

Methods: Data from 35 patients diagnosed with MGRS excluding light-chain amyloidosis between 2013 and 2022 at a single Canadian tertiary care center were retrospectively analyzed. All cases required kidney biopsy. Initial treatment included regimens containing bortezomib, rituximab, or cyclosporine, or steroids only. Parameters studied included incidence of different kidney pathologies, clone type, depth of hematologic response, kidney survival (KS), overall survival (OS), and progression-free survival (PFS).

Results: Out of 35 patients, there were 10 cases of monoclonal immunoglobulin deposition disease, 8 of proliferative glomerulonephritis with immune deposits, 5 of microtubular immune deposits including immunotactoid and types 1 and 2 cryoglobulinemic nephropathy, 3 of C3 glomerulonephritis, and 9 of other diagnoses. There were 21 cases with a plasma cell clone identified in bone marrow, 2 each of B cell and low-grade lymphoma, 1 atypical T cell clone, and 9 cases without an expanded clone on bone marrow biopsy. A total of 6 patients required kidney replacement therapy and 4 patients died; the median PFS was 59.3 months. Very good partial hematologic response or better was significantly associated with decreased proteinuria but not preserved eGFR. There was a non-significant trend toward better PFS with hematologic response.

Conclusion: Our experience confirms that MGRS is a heterogeneous disease and adds to the literature concerning the diagnosis and treatment of MGRS. Successful treatment of the underlying hematologic disorder with targeted therapy is more likely to lead to an improvement in kidney function.

Abrégé

Objectif: La gammapathie monoclonale de signification rénale (MGRS—Monoclonal gammopathy of renal significance) est une affection hétérogène définie relativement récemment qui englobe de nombreuses pathologies rénales et hématologiques. La MGRS demeure une maladie rare, il existe ainsi un besoin de documentation relativement à son traitement et ses résultats. Dans cette étude, nous décrivons l'expérience de notre centre avec la MGRS, notamment l'incidence des différentes pathologies rénales, le type de clone, la réponse rénale et hématologique, et la survie sans progression de la maladie.

Méthodologie: Analyse rétrospective des données de 35 personnes ayant reçu un diagnostic de MGRS sans amylose à chaînes légères entre 2013 et 2022 dans un centre de soins tertiaires au Canada. Tous les cas ont nécessité une biopsie rénale. Le traitement initial comprenait des schémas thérapeutiques de bortézomib, de rituximab ou de cyclosporine, ou des stéroïdes uniquement. Les paramètres étudiés comprenaient l'incidence des différentes pathologies rénales, le type de clone, l'ampleur de la réponse hématologique, la survie rénale (SR), la survie globale (SG) et la survie sans progression (SSP).

Résultats: Parmi les 35 sujets inclus, 10 étaient des cas de maladie par dépôts d'immunoglobulines monoclonales, 8 présentaient une glomérulonéphrite proliférative avec dépôts immunitaires, 5 présentaient des dépôts immunitaires microtubulaires incluant des néphropathies immunotactoïdes et cryoglobulinémiques de types 1 et 2, 3 personnes étaient atteintes de glomérulonéphrite C3 et 9 personnes avaient reçu un autre diagnostic. La cohorte présentait 21 cas de clone plasmocytaire identifié dans la moelle osseuse, deux cas avec lymphome B et deux cas de lymphome de bas grade, un cas de clone de lymphome T atypique, et 9 cas sans clone étendu détecté par biopsie de la moelle osseuse. Au total, six patients

ont nécessité une thérapie de remplacement rénal et quatre personnes sont décédées. La survie médiane sans progression était de 59,3 mois. Une réponse hématologique partielle jugée très bonne ou supérieure a été associée de façon significative à une réduction de la protéinurie, mais sans préservation du débit de filtration glomérulaire estimé (DFGe). Une tendance non significative vers une meilleure survie sans progression a été observée avec une réponse hématologique.
Conclusion: Notre expérience confirme que la MGRS est une maladie hétérogène et enrichit la littérature en lien avec son diagnostic et son traitement. L'utilisation d'une thérapie ciblée pour traiter efficacement le trouble hématologique sous-jacent peut entraîner une amélioration de la fonction rénale.

Keywords
multiple myeloma, paraproteinemias, glomerulonephritis, monoclonal gammopathy of undetermined significance

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What is the New Aspect of Your Work?

We describe our extensive local experience of monoclonal gammopathy of renal significance (MGRS), which is an emerging diagnosis over the last 15 years.

What is the Central Finding of Your Work?

We add to past observations that hematologic response is associated with kidney response and emphasize that MGRS, especially non-amyloid MGRS, is a heterogeneous disease that requires more methods of clinical evaluation.

What is (or Could be) the Specific Clinical Relevance of Your Work?

Our study demonstrates some examples of clone-directed chemotherapy for MGRS, and we show that this can be effective in treating MGRS, which can be important for access to drug coverage.

Introduction

Monoclonal gammopathies of renal significance (MGRS) are a diverse group of disorders characterized by the presence of a monoclonal (M) immunoglobulin (Ig) and kidney injury due to their deposition in the kidney, but which does not fulfill clonal burden criteria for a hematologic malignancy such as multiple myeloma or lymphoplasmacytic lymphoma.1 MGRS also differs from monoclonal gammopathies of undetermined significance (MGUS) as there is an identifiable clinical sequela from the MIg. Monoclonal gammopathy of renal significance include several distinct pathologic entities which have been classified according to their histological appearance: organized, including fibrillar, microtubular, and with inclusions or crystals; non-organized, including monoclonal immunoglobulin deposition disease (MIDD) and proliferative glomerulonephritis with monoclonal immune deposits (PGNMID); and without MIg deposits including C3 glomerulonephritis (C3GN) and thrombotic microangiopathy.2

Monoclonal gammopathy of renal significance is characterized by poor response to immunosuppressive therapy (in contrast to autoimmune nephropathies), a high rate of recurrence after kidney transplant if the monoclonal gammopathy is not eliminated before or immediately after transplantation,3,4 and a risk of progression to hematologic malignancy.2 Thus, treatment for MGRS differs from that of other nephropathies in that it is directed at treating the underlying monoclonal gammopathy. In a recent multi-center study of 280 patients, hematologic response was associated with both kidney response and survival.5

Our center has had a tertiary MGRS referral clinic since 2013 which has seen 35 patients. Here, we describe our experience with regard to diagnosis and treatment of these patients. Initial treatment included regimens containing bortezomib, rituximab, or cyclosporine, or steroids only. Parameters studied included the incidence of different clone types, kidney pathologies, depth of hematologic response, kidney survival (KS), overall survival (OS), and progression-free survival (PFS).

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Patients and Methods

Study Population

The study was approved by the Institutional Review Board at the Tom Baker Cancer Center (TBCC) in Alberta. Between 2013 and 2023, all consecutive patients (a total of 35) who were referred to our MGRS clinic were eligible for retrospective analysis. All patients were diagnosed prior to referral via kidney biopsies. Clone type was determined from bone marrow or lymph node biopsy, which yielded an expanded monoclonal cell line. Chart reviews were conducted to obtain patient demographic data, clinical characteristics including laboratory results, and information regarding treatment regimen. Those with light-chain (AL) amyloidosis, diagnosed based on prior extra-kidney organ involvement, were excluded from the study population.

Response and Survival Assessment

Hematologic response was classified per Palladini et al.6 Complete response (CR) was defined as negative serum and urine immunofixation and normal free light chain (FLC) ratio; very good partial response (VGPR) was defined as the difference between involved and uninvolved light chains (dFLC) below 40 mg/L; and partial response (PR) as dFLC decrease by >50%. Proteinuria response was assessed as a reduction of >30% of 24 h proteinuria (in the absence of kidney progression defined by a progressive decrease of ≥25% of eGFR), including in those with no M protein identified in blood and urine.7

Hematologic progression was defined as a 25% or greater increase in serum M protein (absolute ≥ 0.05 g/L), ≥25% (absolute >200 mg/24 h) increase in urine M protein, or a 50% increase in the difference between involved and uninvolved FLCs (absolute >0.1g/L) or >25% increase in bone marrow plasma cells. Kidney progression was defined as decrease in eGFR of ≥25%. The following data were re-analyzed with this new definition.

Kidney survival (KS) was defined as the length of time from diagnosis to requiring KRT. Overall survival (OS) was defined as the length of time from diagnosis to date of death from any cause. Progression-free survival (PFS) was defined as the length of time from diagnosis to either hematologic progression, KRT, or time of death. Patients who died without disease relapse were censored at the time of death.

Primary Endpoint

The primary endpoint was PFS in patients with VGPR or better vs patients who did not have VGPR or better.

Statistical Analysis

All statistical analyses were performed using the SPSS 28.0 software. P value of $<.05$ was considered statistically significant. Pearson chi-square test was used to compare baseline characteristics and depth of response. Kaplan–Meier method and log-rank tests were used to construct and compare survival curves.

Results

Clinical Characteristics

A total of 35 MGRS patients seen in our clinic between 2013 and 2023 were evaluated. Selected demographics and clinical characteristics are shown in Table 1. Median age of referral was 67 (IQR 58–75.5). Median follow-up was 45.5 months (IQR 15.5–68.7).

Kidney pathologies were categorized based on the IKMG consensus statement on the evaluation of MGRS.2 The most common type of pathology was non-organized Ig deposits (18 in total), made up of 10 cases of MIDD (6 cases of light chain deposition disease (LCDD), 2 of heavy chain deposition disease (HCDD), and 2 of mixed LCDD/HCDD) and 8 cases of PGNMID.

There were 8 cases of organized Ig deposits. These included 5 microtubular Ig deposits (2 of immunotactoid, 2 of type II cryoglobulinemic glomerulonephritis, and 1 of type I cryoglobulinemic glomerulonephritis), 2 of crystalline Ig deposits (1 each of light chain proximal tubulopathy (LCPT) and podocyte crystallopathy), and 1 case of AL/AH amyloidosis.

There were 3 cases of C3GN and 2 cases each of focal segmental glomerulosclerosis and membranous nephropathy observed in the context of MGUS, and there was one case each of anti-glomerular basement disease (GBM) with concurrent IgM MGUS and tubulointerstitial nephritis with IgM deposits on kidney biopsy.

Clone Types and Treatment

Select clinical characteristics stratified by clone type are outlined in Table 2. Out of our 35 patients, there were 21 cases with a plasma cell clone identified in bone marrow, 2 with B-cell clone, 2 with low-grade lymphoma, one with an atypical T cell clone, and 9 cases without an expanded clone on bone marrow biopsy. In the patient with an atypical T cell clone, this patient had anti-GBM disease with concurrent IgM MGUS on kidney biopsy.

The predominant kidney pathology when plasma cell was identified was MIDD (8/21), whereas PGNMID was most common when there was no clone identified (6/9). With regard to KS, 5/21 patients with a plasma cell clone required KRT, whereas all 9 patients with no identified clone avoided KRT.

Table 1. Clinical Characteristics, Including Demographics and Selected Chemistry, of the Total Study Population of Patients With Monoclonal Gammopathy of Renal Significance and Patients With or Without Hematologic Response of Very Good Partial Response (VGPR) or Better.

Clinical characteristics	Total population (n = 35)	Less than VGPR (n = 8)	VGPR or better (n = 16)	VGPR not evaluable (n = 11)
Age in years, median (IQR)	67 (58–75.5)	65 (57.8–74.3)	63 (56–76.3)	69 (62–5.75)
Age ≥ 75 years, n (%)	11 (31.4%)	2 (25%)	5 (31.3%)	4 (36.4%)
Male sex, n (%)	15 (42.9%)	2 (25%)	6 (37.5%)	7 (63.6%)
Monoclonal component				
Heavy chains, n (%)				
IgG κ/λ	15 (42.9%)	5 (62.5%)	4 (25%)	6 (54.5%)
IgG κ	12 (34.3%)	4 (50%)	2 (12.5%)	6 (54.5%)
IgG λ	3 (8.6%)	1 (12.5%)	2 (12.5%)	0 (0%)
IgA κ/λ	2 (5.7%)	0 (0%)	2 (12.5%)	0 (0%)
IgM κ/λ	9 (25.7%)	1 (12.5%)	4 (25%)	4 (36.4%)
Free light chains, n (%)				
κ	20 (57.1%)	5 (62.5%)	11 (68.8%)	4 (36.4%)
λ	6 (17.1%)	2 (25%)	3 (18.8%)	1 (9.1%)
Biclonal	3 (8.6%)	0 (0%)	1 (6.3%)	2 (18.2%)
Lab parameters				
Creatinine (μmol/L), median (IQR)	145 (110–198)	139 (127–198)	158 (125–236)	154 (108–176)
eGFR (mL/min/1.73 m^2), median (IQR)	37 (26–50)	39 (29–51)	35 (25–49)	38 (27–49)
eGFR < 30 mL/min/1.73 m^2, n (%)	11 (31.4%)	2 (25%)	5 (31.3%)	4 (36.4%)
eGFR < 60 mL/min/1.73 m^2, n (%)	29 (82.9%)	6 (75%)	13 (81.3%)	10 (90.9%)
albumin level < 30 g/L, n (%)	18 (51.4%)	4 (50%)	8 (50%)	6 (54.5%)
NT-proBNP > 600 ng/L, n (%)	13 (39.4%)	3 (37.5%)	7 (43.8%)	3 (33.3%)
β2-Microglobulin > 5.5 mg/L, n (%)	11 (34.4%)	3 (37.5%)	5 (33.3%)	3 (33.3%)
24-h urine protein (g), median (IQR)	3 (1.42–6.38)	2.88 (2.26–3.36)	3.33 (1.97–6.31)	3.58 (0.94–9.37)
Lines of treatment, n (%)				
None	1 (2.9%)	0 (0%)	0 (0%)	1 (9.1%)
1 line	25 (71.4%)	3 (37.5%)	13 (81.3%)	9 (81.8%)
2 lines	8 (22.9%)	4 (50%)	3 (18.8%)	1 (9.1%)
3 lines	1 (2.9%)	1 (12.5%)	0 (0%)	0 (0%)
Kidney response, n (%)	26 (74.3%)	4 (50%)	16 (100%)	6 (54.5%)

A total of 34 patients had NT-proBNP measured, and 33 patients had beta 2-microglobulin level measured.
NT-proBNP = N-terminal pro-brain natriuretic peptide; VGPR = very good partial response.

With regard to initial treatment of patients, a total of 20 patients started on bortezomib-containing regimens, 7 patients started on rituximab-containing regimens, 3 patients started on cyclosporine-containing regimens, 2 patients started on steroid-only regimens, and 1 patient was observed due to personal preference. This patient was lost to follow-up at 48 days. A total of 23 patients had only 1 line of therapy, 9 patients had 2 lines of therapy, and 1 patient had 3 lines of therapy. Full details of treatment are included in Supplemental Table 1.

Both initial and final therapy choice were related to the identified clone. Initial treatment in the 21 patients with plasma clone consisted of 18 with bortezomib, 2 steroid-only regimens, and 1 with rituximab, and last treatment for these patients included 11 with bortezomib, 6 with ASCT, and 1 each of rituximab, cyclosporine, steroid only, and daratumumab. In contrast, both patients with identified low-grade lymphoma were started and stayed on rituximab throughout their course. In patients with no identified clone, initial treatment consisted of 4 patients with rituximab, 2 of bortezomib and 1 each of cyclosporine, steroid only, and no treatment due to preference. The final treatment consisted of 5 patients with rituximab, 1 each of bortezomib, cyclosporine, steroid, and untreated.

Hematologic response, as defined by achieving VGPR or better, was best in patients with low-grade lymphoma (2/2) and plasma cell clone identified (11/21). Proteinuria response was also highest in these 2 groups of patients.

Treatment Response and Survival Outcome

With regard to hematologic response, 16 patients (45.7%) achieved VGPR or better. A total of 8 achieved CR, 8 achieved VGPR, 5 achieved PR, 3 achieved no response, and

Table 2. Frequencies, Most Common Immunosuppressive Component of Last Line of Therapy, and Frequency ofVGPR or Better Achieved in MGRS With Different Identified Clone Types.

	Total population (n = 35)	No clone detected (n = 9, 28.6%)	Plasma cell (n = 21, 60%)	B cell (n = 2, 5.7%)	Low-grade lymphoma (n = 2, 5.7%)	Atypical T cell clone (n = 1, 2.9%)
Most common kidney pathology (n, %)	MIDD (10, 28.6%)	PGNMID (6, 66.7%)	MIDD (8, 38.1%)	AL/AH amyloid or immunotactoid (1, 50%)	MIDD (2, 100%)	Atypical GBM (1, 100%)
Most common initial therapy (n, %)	Bortezomib (20, 57.1%)	Rituximab (4, 44.4%)	Bortezomib (18, 85.7%)	Rituximab or corticosteroids (1, 50%)	Rituximab (2, 100%)	Cyclosporine (1, 100%)
Most common last therapy (n, %)	Bortezomib (12, 34.3%)	Rituximab (5, 55.6%)	Bortezomib (11, 52.3%)	Rituximab (1, 50%)	Rituximab (2, 100%)	Cyclosporine (1, 100%)
Patients with VGPR or better, n (%)	16 (44.4%)	3 (33.3%)	11 (52.3%)	0 (0%)	2 (100%)	0 (0%)
Patients with proteinuria response, n (%)	26 (74.3%)	6 (66.7%)	17 (81.0%)	1 (50%)	2 (100%)	0 (0%)
Patients with kidney progression, n (%)	7 (17.1%)	0 (0%)	6 (28.6%)	0 (0%)	0 (0%)	1 (100%)
Patients with death or progression (n, %)	13 (36.1%)	2 (22.2%)	9 (42.9%)	1 (50%)	0 (0%)	1 (100%)
Mean creatinine, mmol/L (range)	171 (44 – 456)	125 (44 – 180)	147 (84 – 209)	188 (86 – 456)	94 (82 – 105)	441

Note. MIDD = monoclonal immune deposition disease; PGNMID = proliferative glomerulonephritis with monoclonal immune deposits; AL/AH = light chain and heavy chain; GBM = glomerular basement membrane disease; VGPR = very good partial response.

hematologic response was not measurable in 11 patients who had no identifiable involved FLC. Six cases proceeded to ASCT at a median time of 6.5 months from diagnosis. Five patients achieved CR and 1 achieved VGPR at day 100. A total of 26 patients achieved proteinuria response. Among patients who had proteinuria response, median time to response was 3 (range 1–12) months. Five patients had a decrease of >50% proteinuria at 6 months.

Among the patients who achieved VGPR, all 16 (100%) achieved proteinuria response; among the patients who did not achieve VGPR, 4 out of 8 (50%) achieved proteinuria response, and 6 out of 11 (54.5%) of patients with unevaluable hematologic response achieved proteinuria response. Hematologic response of VGPR or better was associated with proteinuria response ($P < .001$).

Kidney and PFS curves of the total population are outlined in Figure 1. A total of 7 (20%) patients had kidney progression as defined by ≥25% reduction in GFR 6 months from diagnosis. A total of 4 patients died (range 11.9–64.5 months). A total of 6 patients, 3 of whom initially had proteinuria response, required KRT; mean KS was 87.2 months (95% CI 72.0–102.3). Median KS was not reached. Mean KS was 94.1 months (95% CI 75.9–112.4) in the 2 patients who achieved VGPR and 56.1 months (95% CI 34.3–77.9) in the 3 patients who did not achieve VGPR.

A total of 13 patients had progression, kidney or hematologic, or death. Median PFS was 59.3 months (95% CI 40.9–77.8). KS and PFS stratified by hematologic response (VGPR or better) are found in Figure 2. There was a trend toward better PFS with VGPR in patients whose response was evaluable (mean 74.5 vs 32.8 months, $P = .058$).

Discussion

Monoclonal gammopathy of renal significance is an emerging diagnosis that encompasses a spectrum of kidney diseases associated with the production and deposition of monoclonal immunoglobulins. As a pathologic state of kidney involvement associated with a monoclonal protein but which does not meet the clone burden of an overt hematologic disorder, it is critical to characterize this emerging disease classification for purposes of research and treatment funding.1 Literature to date has included the categorization,2 diagnosis,8,9 clinical progression,10 and treatment5 of MGRS. Our study aimed to highlight our center's experience in the spectrum of presentation and treatment of non-AL amyloidosis MGRS. In particular, we aimed to confirm previous findings that effective treatment of the underlying clone in MGRS is associated with kidney response.5,11,12

Our study adds to the evidence that hematologic response is associated with clinical kidney response in patients with MGRS. We saw a significant association between VGPR or better, a decrease in proteinuria, and a near-significant trend toward improved PFS in these patients. This was also seen in past studies, which showed the same result.5,8 There is a

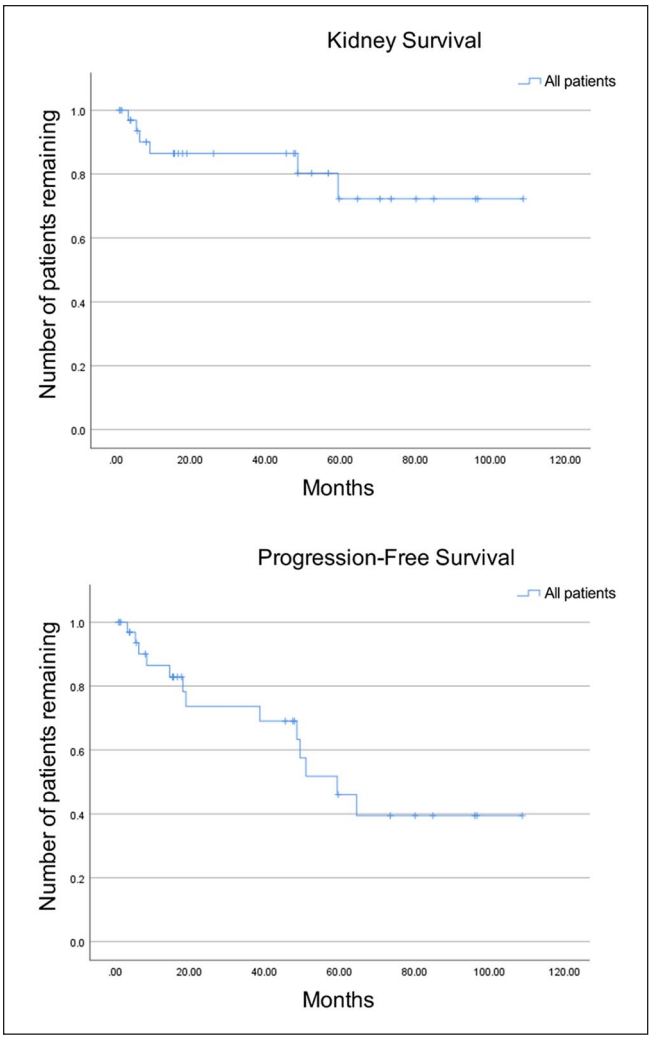

Figure 1. Kidney survival (KS) and progression-free survival (PFS) of the total studied MGRS population (n = 36). Mean kidney survival was 87.2 months (95% CI 72.0–102.3). Median KS was not reached. Median PFS was 59.3 months (95% CI 40.9–77.8). Kidney survival was defined as lack of progression to kidney replacement therapy based on nephrologist clinical judgment. PFS = progression-free survival; KS = kidney survival; MGRS = monoclonal gammopathy of renal significance.

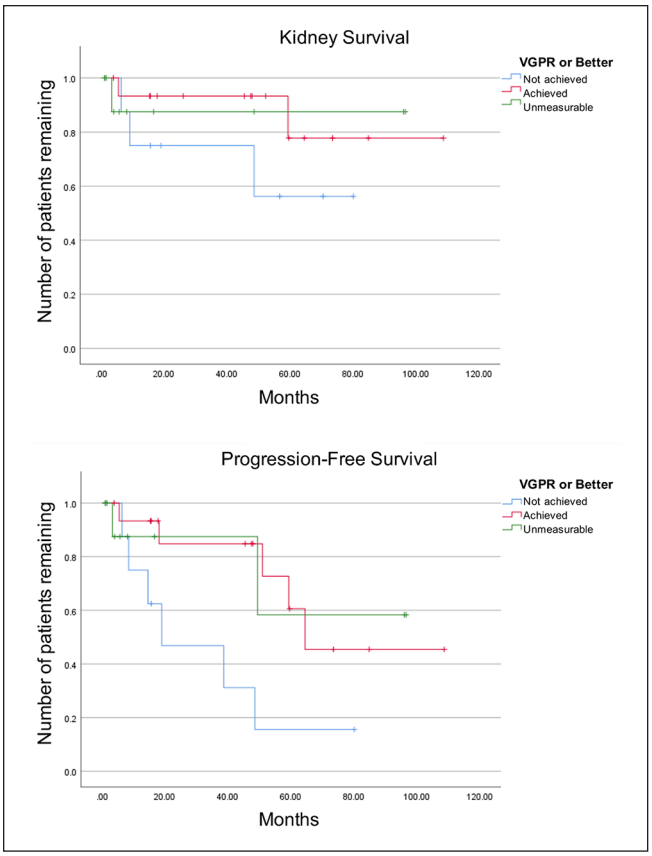

Figure 2. Kidney survival (KS) and progression-free survival (PFS) of the total studied MGRS population (n = 36) depending on hematologic response. A total of 16 patients achieved VGPR or better, 8 did not, and 11 patients were unevaluable. Mean KS of patients was 94.1 vs 84.9 vs 56.1 months, respectively, $P = .417$. Median PFS was 74.5 vs 32.8 vs 71.2 months, respectively, $P = .058$. PFS = progression-free survival; KS = kidney survival; MGRS = monoclonal gammopathy of renal significance; VGPR = very good partial response.

challenge in patients for whom there is no M protein seen in blood or biopsy or no identifiable clone despite the presence of M protein. In our study, there were 11 patients (31.4%) for whom hematologic response was unable to be assessed due to lack of identifiable serum or urine M protein and 9 (25.7%) patients without identified cell clones.

One-half of the patients in our study had either MIDD or PGNMID, while the other half was roughly evenly distributed among other pathologies. We excluded kidney amyloidosis patients from our current study as there are clearer treatment outcomes and response criteria compared to non-amyloidosis MGRS. The reason for this is that kidney amyloidosis may be diagnosed without kidney biopsy; as well, our experience has been that extra-renal involvement often guides assessment of treatment response for these patients.

As a recently described and diverse clinical syndrome, new pathologies comprising MGRS have been described and accepted since the start of our study. These include LCPT, PGNMID, C3GN, and atypical membranous nephropathy.13-16 New techniques including antigen retrieval and immunoEM are not widely used in kidney pathology but may have better sensitivity in detecting these pathologic subclasses.17,18 This could also aid in explaining the high rate of kidney response in patients with no identified bone marrow clone in this paper. While it is important to note that baseline creatinine in the group with no identified clone was lower, another factor could be that our current technologies are not sufficiently sensitive to identify all clones, especially given that half of patients with no identified clone were given rituximab in our experience.

With regard to the distribution of non-amyloidosis kidney pathologies, our observations are similar to those of Gozzetti et al. and Klomjit et al., in that MIDD and PGNMID are relatively common.5,8 We saw a smaller proportion of LCPT (1 case, 2.8%) compared to these other studies. With respect to MIDD and PGNMID, it is interesting to note that MIDD was much more common in patients with an identified plasma cell clone compared to PGNMID, which was more common in patients with no identified clone. This could be reflective of the trend reported by Leung et al. that MIDD occurs more commonly in multiple myeloma than PGNMID (which is mostly restricted to MGRS specifically) (1); a potential mechanism may be that MIDD is associated with a greater tumor burden and thus is more likely to be associated with a detectable cell clone or overt myeloma.

In our center, treatment for MGRS depends on physician discretion. In general, identified plasma cell clones were treated with bortezomib regimens through our jurisdiction's compassionate medication program; on the other hand, patients with B cell and low-grade lymphoma were treated with rituximab. A challenge remains in the treatment of patients without any expanded clone identified, as it is difficult to select a targeted therapy.

An area currently under investigation is the use of mass spectroscopy, most prominently matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF), which is currently endorsed as an emerging alternative to traditional methods such as protein electrophoresis, serum/urine free light chains, or immunofixation.19 MALDI-TOF has demonstrated increased sensitivity to M protein in several plasma cell disorders, including detecting M protein below the threshold of traditional methods of MGUS diagnosis, though it does not seem to have value in patients with established MGUS.20,21 A literature review was not able to identify any studies utilizing MALDI-TOF in patients with PGNMID. As the pathologic diagnosis is most associated with the lack of an identified clone, this would be an important patient population to study the utility of MALDI-TOF.

In our tertiary center, we do not see MGUS managed in primary care or the full spectrum of clinical and subclinical chronic kidney disease. Our clinic, moreover, only saw patients with biopsy-proven MGRS. Additionally, AL amyloidosis was not included in the current study. There thus may be an overrepresentation of clinically significant non-amyloid MGRS studied at our center, and we cannot comment on the true prevalence of the disease. Also, our study remains underpowered as there is a low number of patients. Developing further criteria to raise clinical suspicion of MGRS may help in recruiting more patients for clone-based management and further research.

Considering the high prevalence of MGUS and other pre-malignant monoclonal gammopathies compared to their corresponding overt hematologic malignancies,20 the contribution of MGRS to kidney morbidity in older adults is likely significant. Indeed, 51 patients with MGRS were seen in a tertiary patient population with 1437 total patients with MGUS, smoldering myeloma, and asymptomatic lymphoplasmacytic lymphoma.22 However, the clinical presentations of MGRS can be diverse and heterogeneous, as described in the current and previous studies. More efforts for response criteria assessment, either hematologic or clinical, are needed. This is especially true for patients where no abnormal monoclonal component is noted, who make up a significant portion of the MGRS patient population.

Conclusion

In conclusion, our single-center MGRS patient population remains heterogeneous in terms of kidney pathology and hematologic cell clone, the most common manifestations being LCDD/PGNMID and plasma cell/unknown clone, respectively. Hematologic response was associated with kidney response but only trended with PFS in our study.

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Declaration of Conflicting Interests

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Ethics Approval

The study was approved by the Institutional Review Board at the Tom Baker Cancer Center (TBCC) in Alberta.

Consent to Participate

Monoclonal Gammopathy of Clinical Significance – a Single Center Experience, Ethics approved and active (REB18-1734).

Consent for Publication

All authors provided consent for publication.

Availability of Data and Materials

Data and Materials are available upon request.

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Supplemental Material

Supplemental material for this article is available online.

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