



Original article

Glomerular filtration rate as a prognostic factor in persons with multiple myeloma: A single institution experience

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Abstract

Background: Multiple myeloma (MM) is a malignant plasma cell disorder characterized by the accumulation of abnormal monoclonal plasma cells in the bone marrow. Chronic kidney disease (CKD) is a common complication in patients with multiple myeloma.

Objective: To assess the survival rates among patients with multiple myeloma with any stage of chronic kidney disease treated at the Centro de Hematología y Medicina Interna, Clínica Ruiz, Puebla, México.

Keywords: Multiple myeloma, Chronic kidney disease, Monoclonal proteins, Renal failure, Overall survival, Glomerular filtration rate.

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Materials and methods: Patients with multiple myeloma treated at Clinica Ruiz, Puebla, Mexico, over a 40-year period (1983 to 2023) were analyzed. Age, gender, laboratory data, and treatment features were reviewed. Patients were grouped according to their stage of CKD. The key endpoint was overall survival (OS). Differences in survival were assessed using Kaplan-Meier curves, while changes in glomerular filtration rate (GFR) were evaluated using Student's t-test.

Results: A total of 124 patients were included. Renal damage (stages G2-G5) was present in 68% of patients; the patient distribution was determined as G1 (n=39), G2 (n=40), G3 (n=30), G4 (n=9), and G5 (n=6). Overall survival significantly differed between stage G1 and stages G2-G5 ($p=0.0412$). The median overall survival was not reached for G1, 85.37 months for G2, and 79.8 months for G3. A T-test of glomerular filtration rate before and after treatment showed no significant difference ($p=0.3466$).

Conclusion: Chronic kidney disease is associated with reduced survival in patients with multiple myeloma at any stage.

Tasa de filtración glomerular como factor pronóstico en personas con mieloma múltiple: experiencia de una sola institución

Resumen

Introducción: el mieloma múltiple (MM) es una neoplasia de células plasmáticas caracterizada por la acumulación de células plasmáticas monoclonales anormales en la médula ósea. La enfermedad renal crónica (ERC) es una complicación frecuente en pacientes con mieloma múltiple.

Objetivo: evaluar la supervivencia de los pacientes con mieloma múltiple y cualquier grado de enfermedad renal crónica atendidos en el Centro de Hematología y Medicina Interna, Clínica Ruiz, Puebla, México.

Materiales y métodos: se analizaron pacientes con diagnóstico de mieloma múltiple atendidos en la Clínica Ruiz, Puebla, México, durante un periodo de 40 años (1983–2023). Se revisaron variables demográficas, datos de laboratorio y características del tratamiento. Los pacientes fueron agrupados de acuerdo con el estadio de enfermedad renal crónica. El desenlace principal fue la supervivencia global (SG). Las diferencias en supervivencia se evaluaron mediante curvas de Kaplan-Meier, y los cambios en la tasa de filtración glomerular (TFG) mediante la prueba t de Student.

Resultados: se incluyeron 124 pacientes. El daño renal (estadios G2-G5) estuvo presente en el 68 % de los casos. La distribución fue: G1 (n = 39), G2 (n = 40), G3 (n = 30), G4 (n = 9) y G5 (n = 6). La supervivencia global fue significativamente diferente entre los pacientes con función renal normal (G1) y aquellos con deterioro renal (G2-G5) ($p = 0,0412$). La mediana de supervivencia global no fue alcanzada en G1, mientras que fue de 85,37 meses en G2 y de 79,8 meses en G3. La comparación de la tasa de filtración glomerular antes y después del tratamiento no mostró diferencias estadísticamente significativas ($p = 0,3466$).

Conclusiones: la enfermedad renal crónica se asocia con una disminución de la supervivencia en pacientes con mieloma múltiple, independientemente de su estadio. La función renal al diagnóstico constituye un importante factor pronóstico en esta población.

Palabras clave: mieloma múltiple, enfermedad renal crónica, tasa de filtración glomerular, insuficiencia renal, supervivencia global.

Introduction

Multiple myeloma (MM) is the second most common hematologic malignancy, characterized by a clonal proliferation of plasma B cells and an abnormal increase in monoclonal immunoglobulins due to various post-germinal mutations [1–3]. It is within plasma cell dyscrasias, ranging from monoclonal gammopathy of unknown significance and asymptomatic MM to overt malignant disease (MM and plasma cell leukemia), in which organ damage and associated morbidity occur [4]. MM is more frequent in persons of African ancestry than in Caucasians and slightly more frequent in males than in females [2,5]. It is less frequent in Mexican Mestizo populations than in Caucasians [6].

Approximately 20%-50% of patients with MM have kidney damage at diagnosis due to several factors. Monoclonal light chains can precipitate in the renal tubules, causing light chain cast nephropathy [7,8]. Hypercalcemia, dehydration, the use of nephrotoxic agents, and direct plasma cell infiltration may also contribute to renal impairment, making it an important complication that affects prognosis and quality of life [7].

Due to the high prevalence of kidney damage in persons with MM, it is of utmost importance to understand its impact on the prognosis of patients with MM. The aim of this study was to determine survival among patients with MM with any stage of chronic kidney disease at the Centro de Hematología y Medicina Interna, Clínica Ruiz, Puebla, Mexico.

Materials and methods

Patients were analyzed retrospectively if they had a definitive diagnosis of MM and were treated at Clínica Ruiz, Puebla, México, between 1983 and 2023. The diagnosis of MM was based on the International Myeloma Working Group (IMWG) criteria [9]. Patient medical records were reviewed to collect baseline and follow-up variables of interest, including gender, age, stages of chronic kidney disease, treatment, progression dates, and the date of last follow-up or death.

According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, five groups of patients were analyzed: G1) GFR above 90 mL/min/1.73 m²; G2) GFR of 60 to 89 mL/min/1.73 m²; G3) GFR of 30 to 59 mL/min/1.73 m², including G3a (45-59) and G3b (30-44); G4) GFR of 15 to 29 mL/min/1.73 m²; and G5) GFR less than 15 mL/min/1.73 m² or requiring treatment by dialysis [10]. Patients were divided into two subgroups: 1) Normal renal function: G1; and 2) Abnormal renal function: G2 to G5. The primary endpoint of the study was OS.

The classification of chronic kidney disease (CKD) according to the KDIGO guidelines was used, considering only patients with an estimated glomerular filtration rate (GFR)

<60 mL/min/1.73 m². Regarding the creatinine values used in the subanalysis, measurements were taken at the time of diagnosis and at the end of the treatment, which lasted three months. Patients were treated initially with melphalan/prednisone before 1988; later, they were given thalidomide/dexamethasone, while bortezomib was added for patients who could afford it [11]. Differences between CKD stages were evaluated using Kaplan-Maier survival curves [12]. A comparison of glomerular filtration rate before and after treatment was also performed using Student's t-test in GraphPad Prism software.

Results

A total of 124 patients had complete clinical records and at least a 3-month follow-up period. Normal renal function (G1) was recorded in 39 patients (31%), whereas renal damage (stages G2-G5) was recorded in 85 persons (69%): 40 patients in G2, 30 in G3, 9 in G4, and 6 in G5.

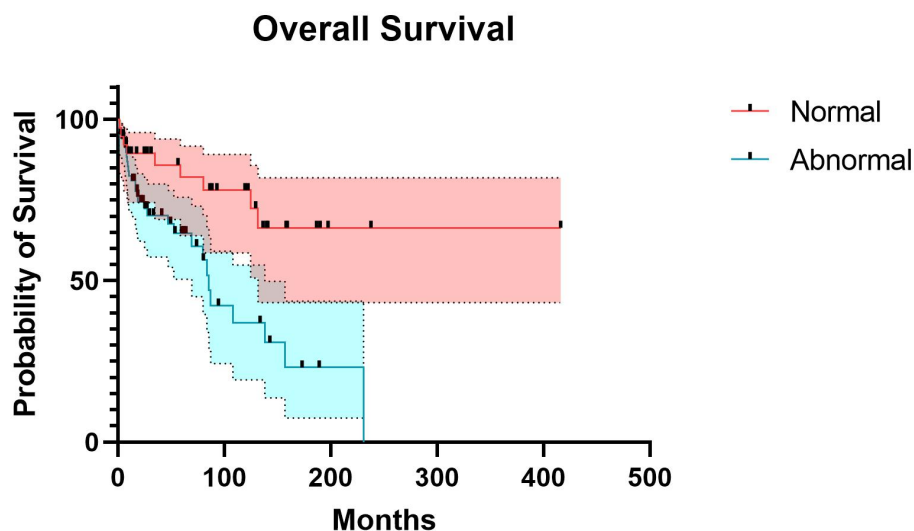
However, within this sub-analysis, when patients were categorized according to the KDIGO criteria for chronic kidney disease and only GFR data were considered, these patients were found to have acute kidney injury rather than chronic kidney disease.

Eighty-four patients received only one line of treatment, whereas 40 received two or more; 51 patients underwent autologous hematopoietic stem cell transplantation (HSCT). The median OS for patients with normal renal function was not reached and exceeded 400 months, whereas the median OS in G2 was 85.4 months ($p=0.04$) (figure 1). OS differed according to the degree of renal damage (figure 2). Stage 3 CKD had the lowest median OS (79.8 months).

A sub-analysis was performed among patients who had at least 3 months of treatment and adequate follow-up ($n=85$), with several determinations of GFR measurements. Changes in GFR were assessed and compared with the baseline values obtained before treatment. The student's t-test was performed, and the difference between the means was found to be not statistically significant ($p=0.35$) (figure 3).

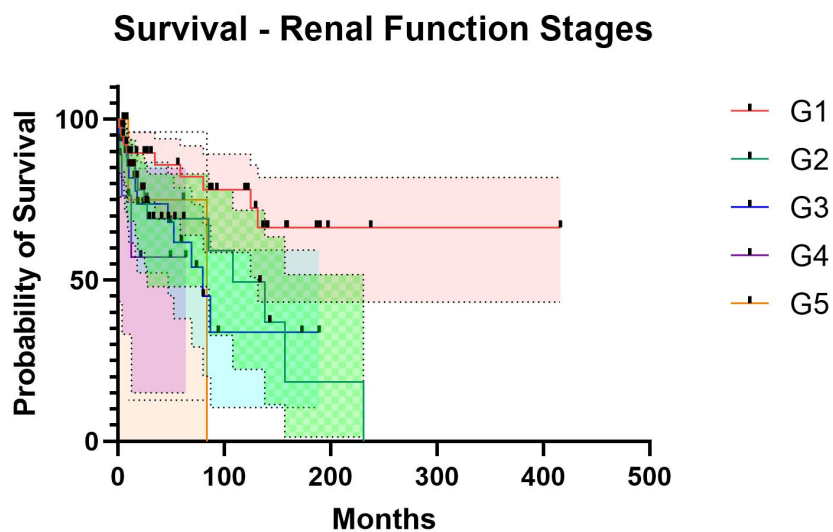
Likewise, within this group, only 5 patients received a bone marrow transplant, and 3 of them had a GFR within normal ranges.

Interestingly, in a subset of 12 patients treated with bortezomib-containing combinations, the GFR improved from a median of 57.25 to 80.4 mL/min/1.73 m²; however, the difference was not statistically significant ($p=0.21$) (figure 4).

Figure 1. Overall survival of multiple myeloma

Note. Patients according to the glomerular filtration rate value at diagnosis (normal or abnormal). The difference is statistically significant ($p=0.04$).

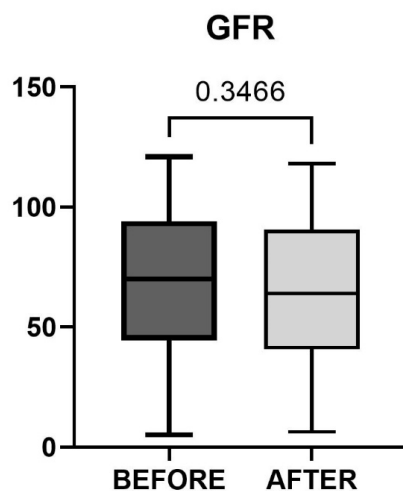
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Figure 2. Overall survival of KDIGO values

Note. Patients with multiple myeloma according to their KDIGO values.

Source: Created by the authors.

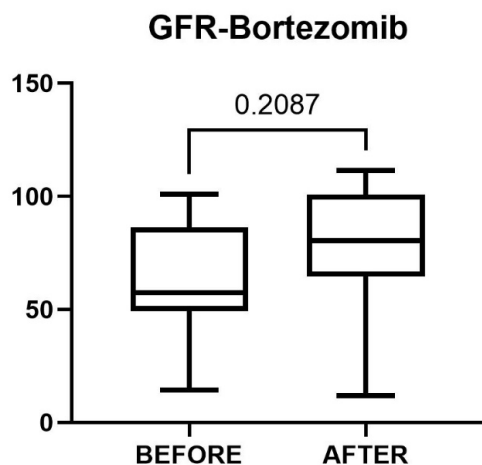
Figure 3. Comparison of glomerular filtration rate (GFR)



Note. GFR values before and after treatment in 85 patients. The difference is not significant according to the Student's t-test.

Source: Created by the authors.

Figure 4. Treatment with Bortezomib



Note. Comparison of glomerular filtration rate (GFR) in patients who were treated with bortezomib-including combinations. The difference is not significant according to the Student's t-test.

Source: Created by the authors.

Discussion

CKD exerts a substantial influence on the survival rates of individuals diagnosed with MM. Renal dysfunction frequently arises as a complication of MM and is associated with an adverse prognosis and elevated mortality risk. Several studies have demonstrated the negative prognostic ramifications of renal dysfunction in MM [13]. Uttervall et al. [14] reported that patients exhibiting renal impairment experienced a median overall survival of 33 months, in contrast to 52 months for those with normal renal function. Courant et al. [15] reported that renal impairment serves as an independent negative prognostic factor, particularly influencing survival outcomes within the initial six months post-diagnosis.

Along this line, our data show that MM patients with normal renal function at diagnosis had a longer overall survival (median above 400 months) compared with patients with compromised renal function (median overall survival of 85 months).

Although CKD adversely affects survival rates in MM, recent advances in therapeutic approaches, particularly the use of novel pharmacological agents and autologous HSCT, have led to enhanced prognostic outcomes for this patient population. Nevertheless, renal dysfunction continues to be a significant determinant influencing clinical prognostic markers [14–16].

In 2013, Kaygusuz et al. examined the renal toxicity associated with bortezomib in a cohort of 56 patients diagnosed with MM, ultimately concluding that a correlation exists between decreased GFR and reduced OS; furthermore, they observed that the exclusive administration of bortezomib may precipitate an increase in both the frequency and severity of adverse events among patients with MM and concurrent renal impairment [17]. There is also data suggesting that bortezomib can reverse the renal damage, which is present in some persons with MM and renal failure at diagnosis [18]. In our small cohort of 12 patients treated with bortezomib, an improvement in glomerular filtration rate was observed; however, the improvement in GFR was not statistically significant ($p=0.21$). Ludwig et al. demonstrated that bortezomib-based treatment led to the reversal of acute paraprotein-related kidney failure in five of eight patients. In every case, renal function improved following a marked decrease in paraprotein levels [18].

The non-significant difference observed in the study may be attributable to the low number of patients in each comparison group, which represents one of the study's limitations, along with its retrospective nature and small sample size.

The prognosis concerning renal functionality in individuals diagnosed with MM exhibits considerable variability among patients; nevertheless, early identification and subsequent intervention can enhance survival rates, particularly when diagnosed in initial stages. The relationship between renal function and MM is complex, as renal impairment constitutes a

notable complication associated with the disease. With regard to the 5 patients who received a bone marrow transplant, 3 of them achieved a GFR within normal parameters; however, this is a significant variable that is associated as a competing factor with favorable survival outcomes.

Conclusion

Renal impairment in patients with MM is a common clinical manifestation of the disease; we found it in 70% of patients. We have also confirmed that renal failure represented itself as a prognostic factor in the OS of patients with a MM diagnosis: survival among MM patients with any degree of renal failure was significantly worse than among patients with normal renal function.

Authors' contributions

Olivia Lira-Lara: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Max Robles-Nasta: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Juan Carlos Olivares-Gazca: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Guillermo José Ruiz-Delgado: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Guillermo José Ruiz Argüelles: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Gloria Erendy Cruz-Pérez: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Moisés Manuel Gallardo-Pérez: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Monica Daniela Salgado-Cabrera: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Miguel Ángel Viveros-Lugo: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Danae García-Velez: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Sofia Chavez-Martínez: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing; Michelle Lavoignet-Cisneros: Conceptualization, formal analysis, investigation, methodology, writing – original draft, writing – review & editing;

Ethical statement

The protocol was approved by the Institutional Review Board of the Clínica Ruiz (CEI-15-01-25-02). Informed consent was obtained from all participants included in the study.

Conflicts of interest

The authors certify that there are no conflicts of interest related to the content of this manuscript. This research did not receive any specific support from public sector agencies, the commercial sector, or non-profit entities.

Funding statement

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Data availability statement

To protect patient confidentiality, the data supporting the findings of this study are not publicly available. The data cannot be shared or distributed because they contain confidential patient information and are protected in accordance with applicable laws and regulations.

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