RESEARCH PAPER

Prognostic Impact of Baseline Renal Dysfunction on Survival in Multiple Myeloma: A Retrospective Cohort Study

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Abstract

Background: Renal dysfunction is a frequent complication of multiple myeloma and may reflect both advanced disease biology and irreversible kidney injury. Its prognostic effect remains clinically important in real-world populations treated with contemporary bortezomib-based regimens.

Methods: This retrospective cohort included 88 patients with multiple myeloma treated at Jawaharlal Nehru Medical College,KAHER,Belagavi,Karnataka ,between January 2019 to December 2025. Baseline renal dysfunction was defined using the laboratory thresholds of serum creatinine >2 mg/dL and/or creatinine clearance <40 mL/min. Pre-existing chronic kidney disease was recorded separately and was not, by itself, sufficient for classification as baseline renal dysfunction. Overall survival (OS) and first-line progression-free survival (PFS-1) were estimated using the Kaplan-Meier method and compared by the log-rank test. Cox proportional hazards regression was used to evaluate factors associated with mortality.

Results: Renal dysfunction was present in 37 of 88 patients (42.05%). The mean age was 61.93 years, 51.14% were male, and 53.41% had International Staging System stage III disease. Median OS was 49.6 months in patients with renal dysfunction and 68.4 months in those without renal dysfunction (log-rank $p<0.001$). One-, two-, three-, and five-year OS estimates were 91.47%, 80.57%, 56.40%, and 37.60% with renal dysfunction, compared with 100%, 100%, 93.84%, and 61.01% without renal dysfunction. Renal dysfunction was associated with mortality on univariable analysis (hazard ratio [HR] 3.72, 95% confidence interval [CI] 1.66-8.32; $p=0.001$) and remained significant after adjustment for ISS stage and lactate dehydrogenase (adjusted HR 3.08, 95% CI 1.30-7.30; $p=0.011$). Median PFS-1 was 22.5 versus 28.0 months, respectively ($p=0.036$).

Conclusion: Baseline renal dysfunction was common and independently associated with inferior OS in this real-world multiple myeloma cohort. The additional association with shorter PFS-1 supports early recognition and rapid myeloma-directed treatment, although prospective studies incorporating estimated glomerular filtration rate, renal recovery, dialysis status, and cause-specific mortality are required.

Keywords: multiple myeloma; renal dysfunction; renal impairment; overall survival; progression-free survival; prognosis

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Introduction

Multiple myeloma is a plasma-cell malignancy characterized by clonal proliferation of plasma cells and myeloma-defining events, including hypercalcemia, renal impairment, anemia, and bone disease. Renal dysfunction is among its most clinically consequential complications because it can arise from light-chain cast nephropathy, light-chain deposition disease, amyloidosis, hypercalcemia, volume depletion, infection, or exposure to nephrotoxic agents. The International Myeloma Working Group (IMWG) currently recommends careful assessment of serum creatinine, estimated glomerular filtration rate, serum free light chains, and urinary protein patterns in patients with suspected myeloma-related kidney injury.[1-3]

Baseline Renal Dysfunction has been reported in approximately 20%-50% of patients at diagnosis, with the highest risk occurring among patients with severe free-light-chain burden, advanced disease, or pre-existing kidney disease.[3,4] Although proteasome inhibitor-based regimens can produce rapid clonal control and meaningful renal recovery, patients presenting with severe renal dysfunction may continue to experience early mortality, treatment complexity, and inferior long-term survival.[2,5-8]

The prognostic literature is not entirely uniform. Several cohort studies have identified severe renal impairment or dialysis dependence as an adverse prognostic factor,[5,7,8] whereas a recent systematic review found that the available comparative evidence was limited and did not establish a consistent difference in OS or PFS between patients with and without renal impairment.[9] Differences in renal definitions, treatment eras, patient selection, and the extent of renal recovery may account for these conflicting findings.

The present study evaluated the prevalence and prognostic association of baseline renal dysfunction in a real-world cohort of 88 patients with multiple myeloma. The primary objective was to determine whether renal dysfunction was associated with OS. Secondary objectives were to evaluate its association with PFS during first-line therapy and to determine whether its prognostic effect persisted after adjustment for ISS stage and lactate dehydrogenase (LDH).

Methods

Study design and setting

This retrospective observational cohort study included 88 patients with multiple myeloma treated at Jawaharlal Nehru Medical College, KAHER, Belagavi, Karnataka, India, between January 2019 and December 2025. Patients were identified through the institutional medical records and oncology database.

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Participants

Patients were eligible if they had a documented newly diagnosed symptomatic multiple myeloma , baseline clinical and laboratory data, first-line treatment information, and survival follow-up. The available dataset included age, sex, socioeconomic status, Eastern Cooperative Oncology Group (ECOG) performance status, comorbidities, CRAB features, ISS stage, laboratory parameters, myeloma subtype, treatment regimen, autologous stem-cell transplantation (ASCT), response, progression, complications, and survival status.

Inclusion Criteria

- Age 18 years or older.
- Confirmed diagnosis of symptomatic multiple myeloma.
- Diagnosis or initiation of first-line treatment during the study period.
- Availability of baseline serum creatinine and renal-function information.
- Availability of first-line treatment and survival follow-up data.

Exclusion Criteria:

- Age < 18 years of age
- Patient with other plasma cell dyscrasis (Smoldering MM, Waldenstroms, Plasmacytoma, POEMS syndrome,plasma cell leukemia,AL Amyloidosis,Insufficient baseline data,insufficient survival follow up)
- Prior history of other malignancy

Renal assessment

Renal dysfunction was recorded as a binary variable in the study dataset and was present in 37 patients. Baseline renal dysfunction was defined as serum creatinine >2 mg/dL and/or creatinine clearance <40 mL/min at the time of multiple myeloma diagnosis or before initiation of first-line therapy. Pre-existing chronic kidney disease was recorded as a separate comorbidity. CKD alone was not considered sufficient for classification as baseline renal dysfunction unless the patient also met the prespecified serum-creatinine or creatinine-clearance threshold. Patients meeting the renal threshold were classified in the baseline renal-dysfunction group regardless of whether they had documented pre-existing CKD.

Treatment

First-line treatment consisted of bortezomib-based triplet regimens: bortezomib-cyclophosphamide-dexamethasone (VCD),

bortezomib-lenalidomide-dexamethasone (VRD), or bortezomib-thalidomide-dexamethasone (VTD). ASCT and maintenance therapy were recorded. Treatment allocation was not randomized.

Outcomes

The primary outcome was OS, defined as the interval from the date of multiple myeloma diagnosis to death from any cause or censoring at the last known follow-up.

PFS-1 was defined as the interval from initiation of first-line therapy to documented disease progression or death from any cause, whichever occurred first.

Progression and response were classified according to **IMWG response criteria.**

Statistical analysis

Normally distributed quantitative variables were summarized using mean and standard deviation, and non-normally distributed variables using median and interquartile range. Categorical variables were summarized as frequencies and percentages. OS and PFS were estimated by the Kaplan-Meier method, with survival distributions compared using the log-rank (Mantel-Cox) test. Median survival and 95% CIs were reported where available. Cox proportional hazards regression was used to estimate HRs and 95% CIs for mortality. Variables with a univariable p value <0.25 were considered for the multivariable model; a parsimonious model was used because only 25 deaths occurred. Statistical significance was defined as a two-sided p value <0.05. Analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Cohort characteristics

The study included 88 patients. Mean age was 61.93 +/- 9.88 years (range, 30-83 years); 45 patients (51.14%) were male and 43 (48.86%) were female. ECOG performance status was 1 in 23 patients (26.14%), 2 in 46 (52.27%), and 3 in 19 (21.59%). Hypertension was present in 35 patients (39.77%), diabetes mellitus in 18 (20.45%), coronary artery disease in 12 (13.64%), and pre-existing CKD in 6 (6.82%),all 6 met the renal-dysfunction threshold.

CRAB features included anemia in 77 patients (87.50%), bone lesions in 58 (65.91%), renal dysfunction in 37 (42.05%), and hypercalcemia in 35 (39.77%). ISS stage I, II, and III disease was present in 16 (18.18%), 25 (28.41%), and 47 patients (53.41%), respectively. Mean serum creatinine was 1.98 +/- 1.53 mg/dL, with a median of 1.30 mg/dL and range of 0.46-9.20 mg/dL. Twenty-six patients (29.55%) had serum creatinine >=2 mg/dL.

All patients received a bortezomib-based first-line triplet: VCD in 30 patients (34.09%), VRD in 27 (30.68%), and VTD in 31 (35.23%). Nine patients (10.23%) underwent ASCT. At the survival cutoff, 63 patients (71.59%) were alive and 25 (28.41%) had died.

Overall survival according to renal dysfunction

Median OS for the entire cohort was 60.5 months. Patients with renal dysfunction had a median OS of 49.6 months, compared with 68.4 months in patients without renal dysfunction. The survival curves were significantly different (log-rank chi-square 11.58; p<0.001; Figure 1).

Estimated OS at one, two, three, and five years was 91.47%, 80.57%, 56.40%, and 37.60%, respectively, among patients with renal dysfunction. Corresponding estimates among patients without renal dysfunction were 100%, 100%, 93.84%, and 61.01%.

Cox regression for mortality

On univariable Cox regression, renal dysfunction was associated with a 3.72-fold higher hazard of death (HR 3.72, 95% CI 1.66-8.32; p=0.001). Normal LDH was associated with a lower mortality hazard compared with elevated LDH (HR 0.30, 95% CI 0.12-0.72; p=0.007). ISS stage III showed a nonsignificant trend toward higher mortality relative to stage I (HR 5.99, 95% CI 0.80-44.96; p=0.082).

In the multivariable model including renal dysfunction, ISS stage, and LDH, renal dysfunction remained independently associated with mortality (adjusted HR 3.08, 95% CI 1.30-7.30; p=0.011). ISS stage and LDH were not statistically significant in the adjusted model, although estimates were imprecise with wide CIs.

First-line progression-free survival

Median PFS-1 was 25.10 months in the overall cohort. Median PFS-1 was shorter in patients with renal dysfunction than in those without renal dysfunction (22.5 versus 28.0 months; log-rank chi-square 4.40; p=0.036; Figure 2). At one, two, and three years, PFS-1 estimates were 74.05%, 39.82%, and 13.27% with renal dysfunction, compared with 89.86%, 61.19%, and 26.21% without renal dysfunction.

Discussion

In this retrospective cohort, renal dysfunction was present in 42.05% of patients with multiple myeloma and was associated with substantially inferior survival. Median OS was approximately 19 months shorter in patients with renal dysfunction, and the adjusted hazard of death was more than three times that of patients without renal dysfunction. Renal dysfunction was also associated with shorter PFS during first-line treatment. These findings identify baseline kidney dysfunction as a clinically important

risk marker in this cohort despite the use of bortezomib-based induction regimens.

The observed prevalence is consistent with reports that kidney impairment affects approximately 20%-50% of patients with newly diagnosed symptomatic myeloma.[3,4,10] Renal dysfunction in myeloma may result from monoclonal free light-chain toxicity, cast nephropathy, glomerular monoclonal immunoglobulin deposition, hypercalcemia, dehydration, infection, and nephrotoxic exposure. It may therefore represent a combination of tumor burden, acute organ injury, pre-existing comorbidity, and reduced physiologic reserve.[2-4]

Our mortality result is concordant with studies demonstrating adverse outcomes in patients with severe renal impairment. Chen and colleagues reported severe renal impairment as an adverse prognostic factor in newly diagnosed myeloma, while multicenter analyses of dialysis-dependent disease have shown high early mortality and shorter OS.[5,7] A 2024 cohort of myeloma patients undergoing ASCT similarly found that moderate-to-severe acute kidney injury was associated with reduced five-year OS.[11] The magnitude of the adjusted association in the current study (HR 3.08) suggests that renal dysfunction retained prognostic information beyond ISS stage and LDH.

Nevertheless, the relationship between renal impairment and myeloma prognosis is complex. A recent systematic review of six studies did not identify a consistent difference in OS or PFS between patients with and without renal impairment, emphasizing the low quality and heterogeneity of the available evidence.[9] Modern proteasome inhibitor, immunomodulatory, and monoclonal antibody-based therapies can produce rapid clonal control and renal recovery, potentially attenuating the historically adverse effect of renal dysfunction.[2,6,10] Differences in renal severity, dialysis status, reversibility, eligibility for intensive treatment, and treatment era are therefore likely to influence results across studies.

The association between renal dysfunction and shorter PFS-1 was less pronounced than its association with OS. One possible interpretation is that kidney dysfunction contributes to mortality through pathways not fully captured by tumor progression, such as infection, cardiovascular disease, electrolyte disturbance, dialysis-related complications, or reduced tolerance of treatment. However, the present dataset did not include cause-specific mortality, treatment dose intensity, dialysis status, or serial renal measurements; this explanation remains hypothesis-generating rather than proven.

All patients received bortezomib-based triplet therapy, consistent with IMWG recommendations that bortezomib-based regimens form the backbone of treatment in myeloma-related renal impairment.[2] Bortezomib-based triplets have been associated with rapid renal responses and dialysis independence in severe renal failure.[6] In the present cohort, first-line regimen was not significantly associated with OS in the supplied survival analysis. That comparison should not be interpreted as evidence of equivalence because treatment was nonrandomized, the sample was small, and regimen selection may have been influenced by renal function, age, frailty, access, and transplant eligibility.

This study has several strengths. It evaluates a clinically important real-world population, includes both OS and PFS outcomes, and demonstrates persistence of the renal association in a parsimonious multivariable model. The observed difference was clinically large, and the renal group represented a substantial proportion of the cohort.

The study also has important limitations. Its retrospective, single-center nature introduces selection bias and limits generalizability. Only 25 deaths occurred, restricting the number of variables that could be reliably included in multivariable analysis and producing wide CIs. The supplied results do not specify the exact operational definition of renal dysfunction, and the numbers classified by renal dysfunction, creatinine >=2 mg/dL, and pre-existing CKD differ. Estimated glomerular filtration rate, creatinine clearance, dialysis requirement, kidney-biopsy findings, proteinuria pattern, serial free light chains, renal response, and durability of renal recovery were not available. Baseline characteristics were not provided separately for renal and nonrenal groups, so residual confounding by age, ECOG status, comorbidities, myeloma subtype, treatment selection, and other disease features cannot be excluded. Moreover, beta-2 microglobulin and ISS stage are influenced by kidney function, complicating interpretation of models that include both staging and renal variables. Cytogenetic risk and cause of death were not reported.

Future work should classify kidney function using a standardized IMWG definition and CKD-EPI estimated glomerular filtration rate, distinguish acute kidney injury from chronic kidney disease, and evaluate renal recovery as a time-dependent exposure. Serial creatinine and free-light-chain measurements would permit assessment of early renal response, dialysis independence, renal trajectories, and whether recovery modifies long-term prognosis.[2,10,12]

Conclusion

Baseline renal dysfunction was common in this multiple myeloma cohort and was independently associated with inferior OS after adjustment for ISS stage and LDH. Renal dysfunction was also associated with shorter PFS during first-line therapy. These findings support rigorous renal assessment at presentation and reinforce the need for rapid, kidney-

conscious myeloma management. Standardized renal definitions and longitudinal renal-response data are required to determine whether early renal recovery can modify the adverse prognosis observed in this cohort.

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Tables

Table 1. Baseline characteristics of the study cohort (N=88)

Characteristic	Value
Age, years, mean +/- SD (range)	61.93 +/- 9.88 (30-83)
Male sex	45 (51.14%)
Female sex	43 (48.86%)
ECOG performance status 1	23 (26.14%)
ECOG performance status 2	46 (52.27%)
ECOG performance status 3	19 (21.59%)
Hypertension	35 (39.77%)
Diabetes mellitus	18 (20.45%)
Coronary artery disease	12 (13.64%)
Pre-existing chronic kidney disease	6 (6.82%)
Anemia	77 (87.50%)
Bone lesions	58 (65.91%)
Renal dysfunction	37 (42.05%)
Hypercalcemia	35 (39.77%)
ISS stage I	16 (18.18%)
ISS stage II	25 (28.41%)
ISS stage III	47 (53.41%)
Serum creatinine, mg/dL, mean +/- SD	1.98 +/- 1.53
Serum creatinine, mg/dL, median (range)	1.30 (0.46-9.20)
Serum creatinine >=2 mg/dL	26 (29.55%)
Elevated LDH	48 (54.55%)
VCD first-line regimen	30 (34.09%)
VRD first-line regimen	27 (30.68%)
VTD first-line regimen	31 (35.23%)

ASCT	9 (10.23%)
Deaths	25 (28.41%)

Data are n (%) unless otherwise stated. ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; LDH, lactate dehydrogenase; VCD, bortezomib-cyclophosphamide-dexamethasone; VRD, bortezomib-lenalidomide-dexamethasone; VTD, bortezomib-thalidomide-dexamethasone; ASCT, autologous stem-cell transplantation.

Table 2. Survival outcomes according to baseline renal dysfunction

Outcome	Renal dysfunction (n=37)	No renal dysfunction (n=51)	p value
Median OS, months	49.6	68.4	<0.001
1-year OS	91.47%	100%	
2-year OS	80.57%	100%	
3-year OS	56.40%	93.84%	
5-year OS	37.60%	61.01%	
Median PFS-1, months	22.5	28.0	0.036
1-year PFS-1	74.05%	89.86%	
2-year PFS-1	39.82%	61.19%	
3-year PFS-1	13.27%	26.21%	

p values are from log-rank tests. OS, overall survival; PFS-1, progression-free survival during first-line therapy.

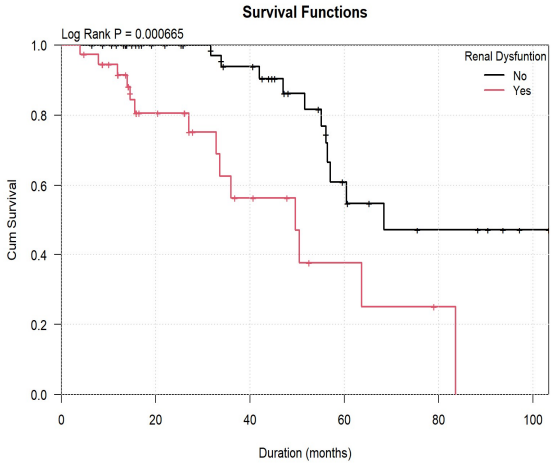
Table 3. Cox proportional hazards regression for overall survival

Variable	Unadjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value
Renal dysfunction: yes vs no	3.72 (1.66-8.32)	0.001	3.08 (1.30-7.30)	0.011
ISS stage II vs I	1.98 (0.23-17.19)	0.534	2.21 (0.26-19.16)	0.471
ISS stage III vs I	5.99 (0.80-44.96)	0.082	2.00 (0.17-23.38)	0.581
Normal vs elevated LDH	0.30 (0.12-0.72)	0.007	0.39 (0.08-1.86)	0.236

HR, hazard ratio; CI, confidence interval; ISS, International Staging System; LDH, lactate dehydrogenase. The adjusted model included renal dysfunction, ISS stage, and LDH.

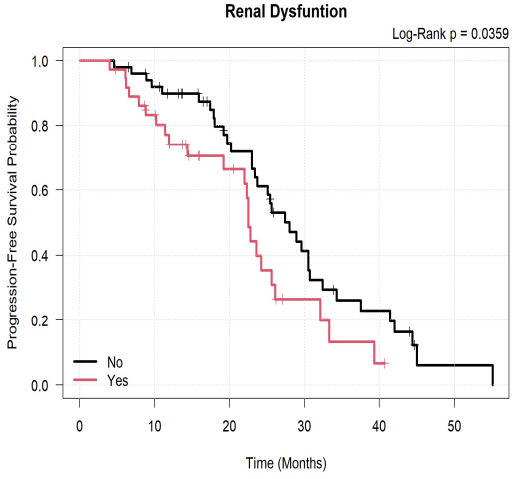
Figures

Figure 1. Kaplan-Meier overall survival according to renal dysfunction



Patients with renal dysfunction had significantly inferior overall survival compared with patients without renal dysfunction (log-rank p<0.001). Add a numbers-at-risk table before submission.

Figure 2. Kaplan-Meier first-line progression-free survival according to renal dysfunction



First-line progression-free survival was shorter in patients with renal dysfunction (log-rank p=0.036). Add a numbers-at-risk table before submission.