Renal impairment in myeloma: Characteristics and outcomes in patients with and without Stage 4 renal impairment in the ANZ Myeloma and Related Diseases Registry

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Background

Multiple myeloma (MM) is a haematologic malignancy of plasma cells associated with morbidities including bone lesions, anaemia, hypercalcemia and renal failure, which are used to define active disease requiring treatment. Renal impairment / failure occurs in up to 40% of myeloma patients[1] and is an independent predictor for poor prognosis[2-4]. We aimed to assess the association of severe renal impairment with higher-risk disease and adverse outcomes in patients with MM on the Australia and New Zealand Myeloma and Related Diseases Registry (MRDR) by comparing characteristics and outcomes of patients with MM and Stage 4 renal impairment[5] (estimated glomerular filtration rate [eGFR] 15-29 mL/min/1.73m2, Table 1) to those with better renal function (eGFR≥30).

Method

Data for all patients with MM registered on the MRDR from 1 Feb 2013 to 19 Jul 2016 were analysed. Of 714 patients with MM, baseline eGFR was available for 623 patients. For 14 patients with baseline serum creatinine alone, eGFR was calculated using baseline creatinine in the Modification of Diet in Renal Disease equation. Patients with an eGFR<15 (End stage renal failure) at baseline were not included in the analysis as dialysis and specialised care can alter outcomes, producing misleading results. Patient characteristics, treatment, response and outcomes were compared between the 2 groups using the Chi squared test for categorical variables, student t-test for normally distributed variables and Wilcoxon rank-sum test for non-normally distributed variables.

Table 1. KDIGO classification of Chronic Renal Disorders[5]

Stage of renal impairment	Description	GFR (mL/min/1.73m²)
1	Kidney damage with normal or elevated GFR	≥ 90
2	Kidney damage with mild reduction of GFR	60-89
3	Moderate reduction of GFR	30-59
4	Severe reduction of GFR	15-29
5	Renal failure	< 15 or on dialysis

Stage 5 is also defined as ESRD, while stage 4 is defined as pre-ESRD
GFR: glomerular filtration rate, ESRD: End stage renal disease

Variable	eGFR 15-29 (n=38)	eGFR ≥30 (n=558)	P-value
Age (median, years)	74 (64-80)	65 (57-74)	<0.001
Age group > 70 years	53% (20/38)	32% (179/558)	0.009
International Staging System = 3	91% (29/32)	22% (93/418)	<0.001
High risk group*	79% (30/38)	33% (183/558)	<0.001
Lactate dehydrogenase, U/L	241 (196-272)	187 (153-240)	0.006
Time from Dx to Rx (median, days)	8 (3-20)	23 (12-42)	<0.001
Time to disease progression (median, months)	15.1 (9-19)	29.6 (19- 40)	0.01
Serum creatinine, µmol/L	224 (193-257)	82 (69-99)	
eGFR	22 (18-27)	78 (60-90)	

Table 2. Comparison of patient characteristics and outcomes between renal function groups . *High risk classification is based on cytogenetics, FISH, LDH & ISS

Results

Of 714 patients with MM, 637 had eGFR available: 41 with eGFR < 15 (End stage renal disease) were not included in the analysis, 38 had eGFR 15 to 29 and 558 had eGFR ≥30. Patients with Stage 4 renal impairment (eGFR 15-29) were older than those with eGFR ≥ 30 (53% >70 years versus 32%, p=0.009), and most were classified with Stage 3 disease on the ISS (79% v 22%, p<0.001) and had higher LDH (241 v 187, p=0.006). Table 2 summarises the differences between groups.

Use of bortezomib is recommended in patients with renal impairment. Bortezomib-based first-line chemotherapy was used in 83% of patients, mixed bortezomib/ thalidomide in 1%, thalidomide in 8%, lenalidomide in 1% and other therapies for 7% of patients (figure 1 provides a comparison between renal function groups). Overall response rate was 68% v 85% (eGFR 15-29 vs eGFR ≥ 30), p=0.03. Response rate for bortezomib-based therapy was 76% v 89%, p=0.03 (Figure 1).

Patients with eGFR 15-29 had a shorter time to disease progression (15.1 v 29.6 months, p<0.001, figure 2). Median overall survival for the cohort was not reached.

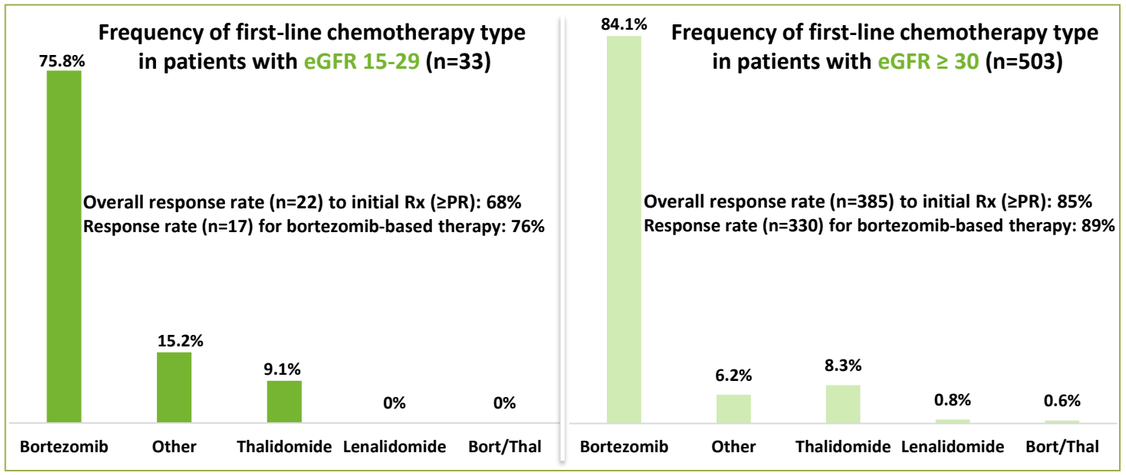
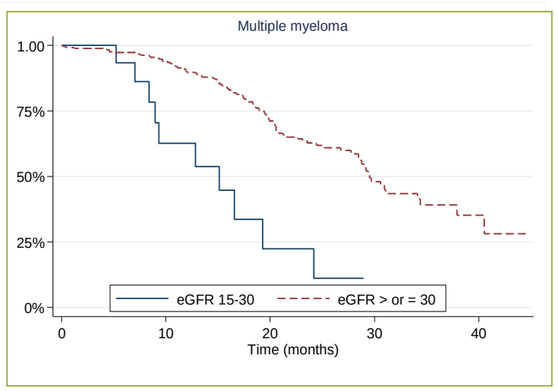


Figure 1. Comparison of frequency of first-line chemotherapy type and response between renal function groups (n=536)

Conclusion

Renal morbidity from MM is a considerable burden. In our cohort, patients with severe renal impairment had higher-risk disease and poorer outcomes. Even in the 'bortezomib era', stage 4 renal impairment (eGFR 15-29) is strongly associated with poor prognosis. This data suggests that greater vigilance is needed in patients with eGFR 15-29.

Figure 2. Time to disease progression in patients with MM: eGFR 15-29 versus ≥30



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A C B D Australian Centre for Blood Diseases

TheAlfred