Clinical implications and predictive value of the creatinine-cystatin C ratio in patients with multiple myeloma and renal impairment

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Abstract. The creatinine (Cr)-cystatin C ratio (CCR) at the time of cancer diagnosis is associated with survival; however, to the best of our knowledge, the association between this ratio and mortality in patients with multiple myeloma and renal impairment (RI) is unclear. Therefore, the present study aimed to assess this association, as well as disease prognosis and the clinical significance of the CCR in patients with multiple myeloma and RI. The present retrospective study included 191 patients diagnosed with multiple myeloma and RI between 2012 and 2022. The predictive value of the CCR was evaluated using area under the receiver operating characteristic curve (AUC) values. The factors affecting overall survival (OS) were assessed using uni- and multivariate logistic regression analyses. The effect of the CCR on survival was evaluated using a Cox regression model and the Kaplan-Meier method. There was a significant association between low CCR and poor progression-free survival (PFS) and overall survival (OS). The 1-, 2- and 3-year PFS and OS rates in patients with a low CCR were significantly lower than those in patients with a high CCR. The 1-, 2- and 3-year AUC values of the CCR were 0.712, 0.764 and 0.746 respectively. Multivariate analysis revealed sex, age, Cr levels, CCR and C-reactive protein levels as independent prognostic factors affecting OS rates. The CCR is a potential prognostic indicator in patients with multiple myeloma with RI and is associated with clinical stages.

Introduction

Multiple myeloma is the second most common hematological malignancy and is characterized by neoplastic proliferation of monoclonal plasma cells (1,2). It accounts for ~10% of hematological malignancies and 1% of all cancer cases globally (3). The current standard of treatment is the bortezomib regimen, administered in combination with dexamethasone and an immunomodulatory drug (thalidomide or lenalidomide). Most patients have an effective response to these regimens and ~50% have at least a partial response (4). Following autologous stem cell transplantation (ASCT), the degree of response increases (4). As a result, ASCT remains the standard of care in many parts of the world. CD38-targeting antibodies (daratumumab and isatuximab) are emerging as a key component of relapse and first-line therapy (5). However, systemic therapy is generally not initiated until myeloma-associated symptoms such as anemia, hypercalcemia, bone disease or renal damage are observed (3,6,7). Despite advances in the treatment of multiple myeloma, it remains an incurable disease (8). Therefore, characteristics of multiple myeloma require further exploration and the identification of effective prognostic biomarkers is needed to maximize survival in patients with this disease.

As a common complication in patients with multiple myeloma, renal impairment (RI) is an independent factor indicating poor prognosis (6,9,10) and is associated with shortened

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treatment time and overall survival (OS) (11). Accurate identification of concomitant renal damage is key as recovery from RI is associated with the treatment response (11). In general, RI is determined based on a decrease in creatinine (Cr) clearance or increase in serum Cr (sCr) levels (12-14). However, both parameters are imprecise and underestimate RI. Thus, they do not represent the most accurate method for evaluating RI, especially in elderly patients with malnutrition and fragility, which are common features in patients with multiple myeloma (12-14). Kidney Disease Improving Global Outcomes guidelines recommend calculations based on a combination of sCr and cystatin C (CysC) to estimate the glomerular filtration rate in patients with RI (15). sCr and CysC are commonly used markers to evaluate glomerular filtration (16). sCr is affected by multiple factors, including muscle mass, medications and diet (17), whereas CysC, derived exclusively from all nucleated cells and mildly metabolized by muscle tissue, is used to estimate glomerular filtration function regardless of lean body mass and nutritional status (18,19). The Cr-CysC ratio (CCR) in the peripheral blood can be used to predict the prognosis in patients with cancer such as esophageal cancer (18,20). Therefore, CCR may be a promising prognostic indicator in patients with multiple myeloma with RI. However, this method must be validated before it can be widely implemented in clinical practice.

To the best of our knowledge, there are no studies on the association between the CCR and prognosis in patients with multiple myeloma and RI. Therefore, the present study aimed to assess clinical implications and the predictive value of the CCR in these patients.

Materials and methods

Study design and participants. The present retrospective analysis included 191 patients who were newly diagnosed with multiple myeloma with RI between January 2012 and December 2022 at Shandong Provincial Hospital Affiliated with Shandong First Medical University (Jinan, China). There were 103 male (53.9%) and 88 female (46.1%). Patients were between the ages of 18 and 80 years. Among them, 55 (28.8%) were older than 65 years. The mean age of all patients was 62 years. Inclusion and exclusion criteria are listed in Fig. 1. For patients who were hospitalized multiple times during the study period, only the first hospitalization record was used. The present study complied with the provisions of the Declaration of Helsinki and was approved by the Ethics Committee of the Shandong Provincial Hospital Affiliated with Shandong First Medical University (Jinan, China), which waived the requirement for informed consent due to the retrospective study design (approval no. SWYX2023-582).

Data collection. Demographic and laboratory data were retrieved from electronic databases and patient medical records. The collected data included the following: i) General information, including age and sex; ii) underlying disease, including hypertension, diabetes mellitus and coronary heart disease; iii) laboratory tests, including bone marrow plasma cell proportion, hemoglobin, platelet count, sCr, CysC, C-reactive protein (CRP), albumin, β-2-microglobulin (β-2-MG) and lactate dehydrogenase (LDH); and iv) pathological information, including bone destruction. The presence of bone destruction was detected using positron emission tomography-CT and body CT or magnetic resonance imaging. The following formula was used to calculate the CCR: sCr/serum CysC (mg/l).

Follow-up and outcomes. The patients were regularly followed up after discharge. The follow-up monitoring included regular visits to in-patient clinics and telephone interviews. The patients were followed up every 3-6 months in the first year and every 6-12 months from the second year until death. The follow-up evaluations included questions about basic living conditions, serum examination results and bone marrow plasma cell proportions. Progression-free survival (PFS) was calculated from the time of diagnosis to disease progression or death from any cause. OS was estimated as the time from diagnosis to death. The final follow-up was performed in July 2023.

Statistical analysis. R software version 4.0.3 (R-project.org) was used to perform the statistical analysis. All data are expressed as mean ± standard deviation. The probabilities of PFS and OS were calculated using the Kaplan-Meier method and the Log rank test was used for comparison. And uni- and multivariate Cox regression models were used to evaluate the risk factors affecting prognosis in patients with multiple myeloma. Continuous variables were compared using an unpaired Student's t-test and the Wilcoxon rank-sum test and categorical variables were compared using the χ^2 test. All tests were two-sided and $P<0.05$ was considered to indicate a statistically significant difference. Receiver operating characteristic (ROC) curves were used to evaluate the ability of CCR to predict mortality, and X-tile software version 3.6 (http://x-tile.software.informer.com) was used to determine the optimal cut-off point. The predictive accuracy of the CCR was determined using the area under the ROC curve (AUC). Subsequently, patients were classified into two groups (high and low) based on the CCR cut-off value (1.31).

Results

CCR and clinical parameters at baseline. Overall, 191 patients were eligible for inclusion. The baseline clinical characteristics of patients are shown in Table I. The study population included 55 (28.8%) patients aged >65 years and 136 (71.2%) aged ≤65 years; 103 (53.9%) patients were male. Regarding the multiple myeloma stage, 85 (44.5%) patients had DS stages I-II disease, 106 (55.5%) DS stage III, 74 (38.7%) ISS stages I-II, 117 (61.3%) ISS stage III, 80 (41.9%) R-ISS stages I-II, and 111 (58.1%) R-ISS stage III disease. Bone lesions were observed in 125 patients (65.4%). Light chain-λ type was observed in 37 (19.4%) of cases, light chain-κ type in 33 (17.3%), IgA-λ type in 35 (18.3%), IgA-κ type in 16 (8.4%), IgD-λ type in 4 (2.1%), IgD-κ type in 33 (17.3%) and IgG-λ type in 33 (17.3%). All patients received bortezomib-based chemotherapy at 1.3 mg/m^2 for 4-6 cycles on days 1, 4, 8 and 11 of a 3-week cycle. A total of 19 patients received palliative care due to chemotherapy intolerance or economic constraints.

ROC curves evaluating the ability of the CCR to predict mortality are shown in Fig. 2. The 1-, 2- and 3-year AUC values for CCR were 0.712, 0.764 and 0.746 respectively. The optimal

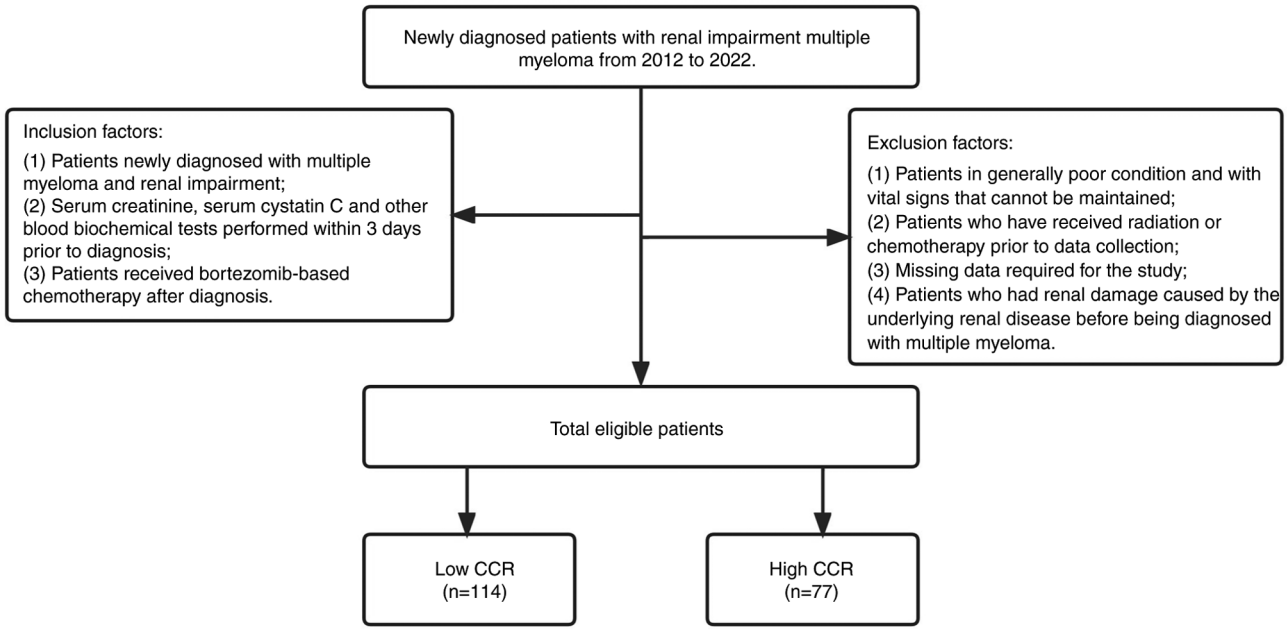

Figure 1. Study flowchart. CCR, creatinine-cystatin C ratio.

critical value of CCR for predicting the prognosis in patients with multiple myeloma with RI was 1.31, corresponding to a sensitivity and specificity of 76.7 and 71.5%, respectively. Subsequently, participants were divided into low (CCR, <1.31; n=114; 59.7%) and high (CCR, ≥1.31; n=77; 40.3%) CCR groups (Table I). The median follow-up time in all patients was 42 months (range, 6-97 months). CCR was significantly associated with sex, clinical type, high bone marrow plasma cell levels, bone lesion, hemoglobin, platelet, calcium and Cr levels, urea nitrogen, β-2-MG, albumin, CRP and LDH levels, 24-h urinary protein quantity, and ISS and R-ISS stage. No significant differences in age, erythrocyte sedimentation rate, CysC levels or DS stage were observed between groups.

Uni- and multivariate analysis of OS. The survival of patients with high CCR was longer than that of patients with low CCR. In univariate Cox proportional hazard regression models, OS were significantly associated with female sex, age >60 years, absence of bone lesions, low Cr levels, CCR, low urea nitrogen and β-2-MG levels, high CRP levels, low 24-h urinary protein quantity and DS stage I-II (Table II). Multivariate analysis of the 10 significant factors in the univariate analysis demonstrated that independent prognostic factors associated with OS in patients with multiple myeloma were sex [hazard ratio (HR), 0.325; 95% CI, 0.19-0.556], age (HR, 2.349; 95% CI, 1.471-3.749), Cr levels (HR, 0.396; 95% CI, 0.212-0.736), CCR (HR, 0.35; 95% CI, 0.19-0.646) and CRP levels (HR, 3.02; 95% CI, 1.71-5.335; Table II).

Association between CCR and clinical stage in patients with newly diagnosed multiple myeloma and RI. The CCR range in 191 patients with newly diagnosed multiple myeloma and RI was 0.127-4.310, with a median value of 0.977. A total of 114 (60%) had a CCR <1.31. Patients with clinical stages I or II were combined into one group due to the low number of patients in each group; ~71.1% of patients (81/114) with R-ISS stage III had a low CCR, whereas ~28.9% (33/114) of patients with R-ISS stage I-II had a low CCR (Table I). The CCR differed significantly between patients with R-ISS stages I-II and III (Fig. 3A). For patients with ISS stage III, ~73.7% (84/114) had a low CCR (Table I). A higher ISS stage was more likely to be associated with a low CCR. The CCR differed significantly between patients with ISS stages I-II and III (Fig. 3B), as well as between patients with DS stages I-II and III (P<0.05; Fig. 3C). When the CCR was a continuous variable, DS showed a significant difference (Table II); however, when the CCR value is delimited by 1.31 as the categorical variable, the difference was not significant (Table I).

Kaplan-Meier survival curves of association of CCR with OS and PFS. During the follow-up period, 103 (53.9%) patients died, including 60 (58.3%) in the low CCR group and 43 (41.7%) in the high CCR group. Kaplan-Meier survival curves demonstrated significantly lower 1-, 2- and 3-year PFS rates in patients in the low CCR compared with those in the high CCR group (Fig. 4A). Furthermore, patients with a low CCR had significantly lower 1-, 2- and 3-year OS rates than those with a high CCR (Fig. 4B). PFS was significantly lower in patients with R-ISS stage III disease and low CCR compared with in those with a high CCR, with significant differences observed at 1, 2 and 3 years (Fig. 5A). The OS in patients with R-ISS stage III disease with a low CCR was significantly lower than that in patients with a high CCR, with significant differences observed at 1 and 2 years (Fig. 5B). The PFS in patients with ISS stage III disease with a low CCR was significantly lower than that in patients with a high CCR, with significant differences at 1, 2 and 3 years (Fig. 5C). The OS in patients with ISS stage III disease with a low CCR was significantly lower than that in patients with a high CCR, with significant differences at 1, 2 and 3 years (Fig. 5D). The PFS in patients with DS stage III disease with a low CCR was significantly lower than that in patients with a high CCR, with significant

Table I. CCR and clinical parameters at baseline.

Characteristic	CCR <1.31, n (%) (n=114)	CCR ≥1.31, n (%) (n=77)	P-value
Sex			<0.01
Male	38 (33.33)	65 (84.41)	
Female	76 (66.66)	12 (15.58)	
Age, years			0.99
>65	33 (28.94)	22 (28.57)	
≤65	81 (71.05)	55 (71.42)	
Clinical type			<0.01
IgA-κ	15 (13.15)	1 (1.29)	
IgA-λ	30 (26.31)	5 (6.49)	
IgD-λ	3 (2.63)	1 (1.29)	
IgD-κ	19 (16.66)	14 (18.18)	
IgG-λ	27 (23.68)	6 (7.79)	
κ	9 (7.89)	24 (31.16)	
λ	11 (9.64)	26 (33.76)	
BMPC, %)			<0.01
>30	29 (25.43)	37 (48.05)	
≤30	85 (74.56)	40 (51.94)	
Bone lesion			<0.01
Yes	56 (49.12)	69 (89.61)	
No	58 (50.87)	8 (10.38)	
Hemoglobin, g/l			<0.01
>85	58 (50.87)	18 (23.37)	
≤85	56 (49.12)	59 (76.62)	
Plt, x10^9/l			<0.01
>300	18 (15.78)	2 (2.59)	
≤300	96 (84.21)	75 (97.40)	
Calcium, mg/dl			0.03
>2.8	10 (8.77)	15 (19.48)	
≤2.8	104 (91.22)	62 (80.51)	
Creatinine, μmol/l			<0.01
>177	86 (75.43)	45 (58.44)	
≤177	28 (24.56)	32 (41.55)	
Cystatin C, mg/l			0.05
>1.6	94 (82.45)	71 (92.20)	
≤1.6	20 (17.54)	6 (7.79)	
Urea nitrogen, mmol/l			<0.01
>7.1	88 (77.19)	77 (100.00)	
≤7.1	26 (22.80)	0 (0.00)	
β-2-microglobulin, mg/l			<0.01
>5.5	27 (23.68)	45 (58.44)	
≤5.5	87 (76.31)	32 (41.55)	
Albumin, g/l			<0.01
>35	34 (29.82)	38 (49.35)	
≤35	80 (70.17)	39 (50.64)	

Table I. Continued.

Characteristic	CCR <1.31, n (%) (n=114)	CCR ≥1.31, n (%) (n=77)	P-value
C-reactiveprotein, mg/l			<0.01
>10	31 (27.19)	15 (19.48)	
≤10	83 (72.80)	62 (80.51)	
LDH, U/l			0.02
>247	11 (9.64)	26 (33.76)	
≤247	103 (90.35)	51 (66.23)	
24-h urinary protein, g			0.03
>0.15	107 (93.85)	77 (100.00)	
≤0.15	7 (6.14)	0 (0.00)	
ESR, mm/h			0.09
>20	105 (92.10)	65 (84.41)	
≤20	9 (7.89)	12 (15.58)	
ISS stage			<0.01
I-II	30 (26.31)	44 (57.14)	
III	84 (73.68)	33 (42.85)	
DS stage			0.23
I-II	40 (35.08)	45 (58.44)	
III	74 (64.91)	32 (41.55)	
R-ISS stage			<0.01
I-II	33 (28.94)	47 (61.03)	
III	81 (71.05)	30 (38.96)	

CCR, creatinine-cystatin C ratio; BMPC, bone marrow plasma cell; Plt, platelet; LDH, lactate dehydrogenase; ESR, erythrocyte sedimentation rate; ISS, International Staging System; DS, Durie-Salmon staging system; R-ISS, revised ISS.

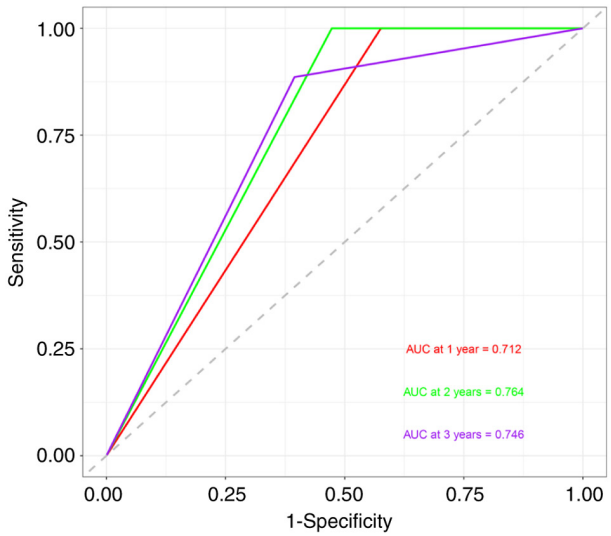

Figure 2. Receiver operating characteristic curves demonstrating ability of creatinine-cystatin C ratio to predict mortality. AUC, area under the receiver operating characteristic curve.

Table II. Uni- and multivariate Cox regression analyses of OS.

	Univariate		Multivariate	
Characteristics	HR (95% CI)	P-value	HR (95% CI)	P-value
Female	0.463 (0.312-0.687)	0.005	0.325 (0.190-0.556)	0.001
Age >60 years	1.569 (1.047-2.350)	0.029	0.349 (0.471-0.749)	0.003
BMPC <30%	0.958 (0.640-1.432)	0.833	1.198 (0.512-1.967)	0.734
Absence of bone lesions	0.629 (0.422-0.938)	0.023	0.962 (0.690-1.372)	0.874
Hemoglobin >85 g/l	1.229 (0.829-1.823)	0.305	0.839 (0.411-1.430)	0.382
Plt ≤300x10^9/l	0.735 (0.357-1.514)	0.404	0.835 (0.426-1.317)	0.305
Calcium >2.8 mg/dl	1.098 (0.611-1.972)	0.754	1.149 (0.769-1.813)	0.406
Creatinine <177 μmol/l	0.583 (0.385-0.881)	0.010	0.396 (0.212-0.736)	0.012
Cystatin C <1.6 mg/l	0.749 (0.371-1.510)	0.419	0.627 (0.451-1.510)	0.314
CCR <1.31	0.389 (0.260-0.580)	0.002	0.350 (0.190-0.646)	0.002
Urea nitrogen ≤7.1 mmol/l	0.443 (0.267-0.443)	0.001	0.525 (0.347-0.553)	0.061
β-2-microglobulin <5.5 mg/l	0.465 (0.298-0.727)	0.003	0.675 (0.468-0.637)	0.072
Albumin ≤35 g/l	0.845 (0.565-1.262)	0.412	0.645 (0.735-1.564)	0.536
C-reactive protein >10 mg/l	2.383 (1.581-3.592)	0.005	3.020 (1.710-5.335)	0.005
LDH <247 U/l	0.769 (0.475-1.244)	0.284	0.649 (0.365-1.124)	0.301
24-h urinary protein <0.15 g	0.343 (0.157-0.749)	0.007	0.641 (0.557-0.949)	0.061
ESR >20 mm/h	1.524 (0.739-3.139)	0.254	1.164 (0.549-1.214)	0.367
ISS stage I-II	0.744 (0.541-1.023)	0.069	0.864 (0.873-1.426)	0.072
DS stage I-II	0.755 (0.616-0.925)	0.014	0.624 (0.356-0.867)	0.071
R-ISS stage I-II	0.935 (0.689-1.300)	0.689	0.845 (0.532-1.779)	0.724

HR, hazard ratio; BMPC, bone marrow plasma cell; Plt, platelet; CCR, creatinine-cystatin C ratio; LDH, lactate dehydrogenase; ESR, erythrocyte sedimentation rate; ISS, International Staging System; DS, Durie-Salmon staging system; R-ISS, revised ISS.

differences at 1, 2 and 3 years (Fig. 5E). The OS in patients with DS stage III disease and low CCR was significantly lower than that in patients with a high CCR. Significant differences were observed at 1,2 and 3 years (Fig. 5F). Due to the small number of patients with clinical stage I-II, survival analysis in this subgroup was not performed.

Discussion

The present study suggested that the CCR is an important predictor of PFS and OS in patients with multiple myeloma and RI. The survival rate in patients with multiple myeloma was increased with increased CCR. The CCR may also be an effective auxiliary tool for staging to predict prognosis in patients with multiple myeloma at the same stage (Table I). Furthermore, there were significant differences in the CCR at different stages of DS, ISS and R-ISS. The AUC values of the 1-, 2- and 3-year ROC curves for the prediction of mortality and prognosis were 0.712, 0.764 and 0.746, respectively. The optimal cut-off of the CCR was 1.31, Furthermore, multivariate logistic regression analysis revealed that CCR <1.31 was an independent risk factor for prognosis after adjusting for confounding factors. These results demonstrated the potential of the CCR as a predictor of prognosis in hospitalized patients with multiple myeloma with RI. Furthermore, CCR value could predict the prognosis among patients with different clinical stages.

RI is a common complication associated with poor prognosis in multiple myeloma (11). sCr and CysC levels are widely used as endogenous markers to assess glomerular filtration function (21). Cr is an end product of muscle catabolism, which is affected by muscle mass and protein intake and varies according to patient age and sex and the presence of chronic disease (22,23). Serum CysC levels can accurately and quickly reflect several types of renal insufficiency. Furthermore, certain CysC genotypes are associated with the occurrence and development of malignant tumors, which are influenced by gene polymorphisms (24,25). In the present study, multi-factor analysis revealed that CysC was not an independent prognostic factor for patients with newly diagnosed multiple myeloma, which was consistent with the findings of Zhang *et al* (26). However, this contradicts the findings of Nückel *et al* (27) and Terpos *et al* (28). The conflicting results may be due to the limitations of the retrospective study design and relatively small sample size of the present study. As the CCR was an independent risk factor in the multi-factor analysis, it showed a greater predictive power than CysC. In recent years, the association between the CCR and prognosis in patients with cancer has attracted increasing attention: Jung *et al* (29) and Zheng *et al* (20) reported that the CCR is a useful prognostic factor for long-term survival in patients with cancer. Chen *et al* (30) reported that the CCR is associated with mortality in female, but not male, patients with non-small cell lung cancer. Gao *et al* (31) reported that patients with a high

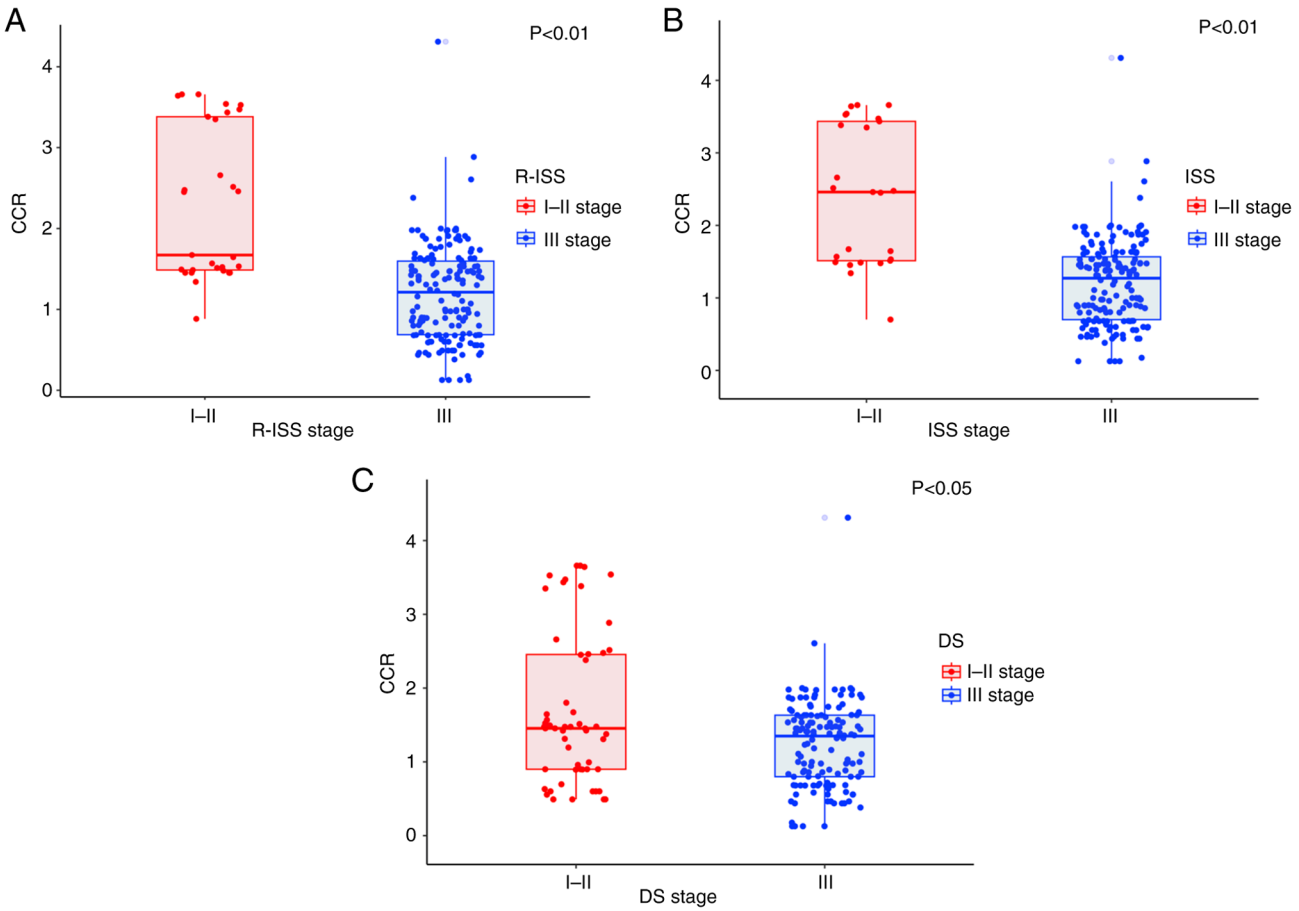

Figure 3. CCR in different clinical stage patients with multiple myeloma. Differences in CCR between patients with multiple myeloma with (A) R-ISS stages I-II and III (P<0.01), (B) ISS stages I-II and III (P<0.05), and (C) DS stages I-II and III (P<0.05). CCR, creatinine-cystatin C ratio; DS, Durie-Salmon staging system; ISS, International Staging System; R-ISS, revised ISS.

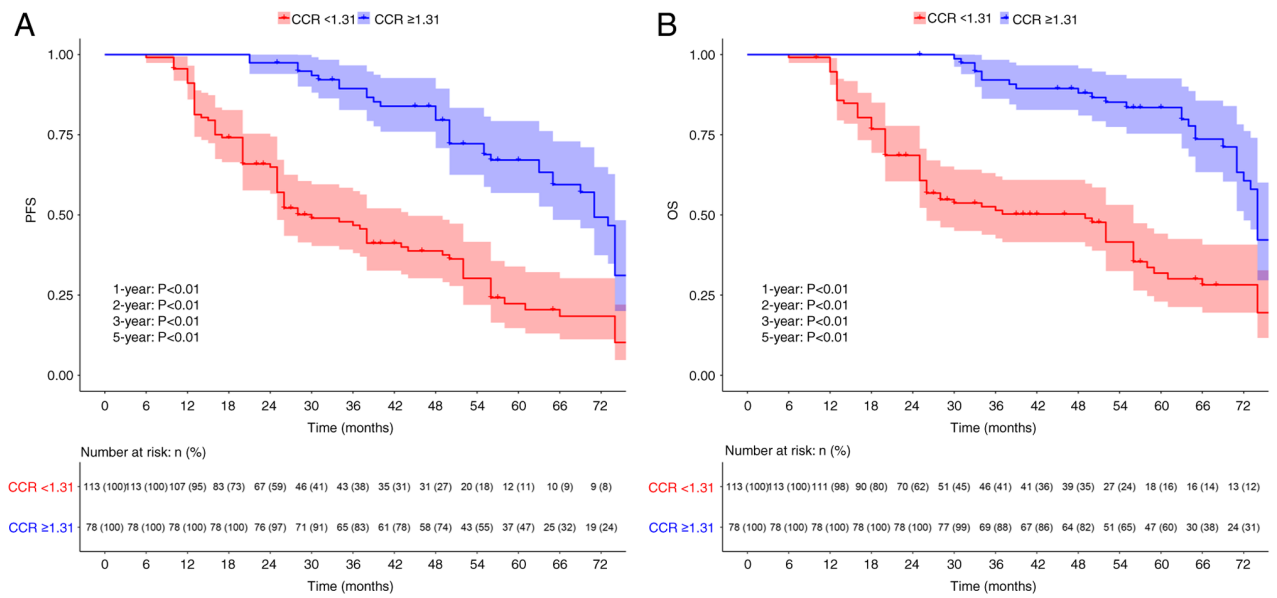

Figure 4. Kaplan-Meier curves demonstrating association between CCR in patients with multiple myeloma and renal impairment and PFS and OS. (A) PFS. (B) OS. CCR, creatinine-cystatin C ratio; OS, overall survival; PFS, progression-free survival.

CCR have a notably higher relapse-free survival time and OS than those with a low serum CCR. These results are consistent with the findings of the present study. Chen *et al* (30) reported that the CCR is an independent risk factor for in-hospital mortality in patients hospitalized for acute exacerbation of chronic obstructive pulmonary disease: The AUC value for

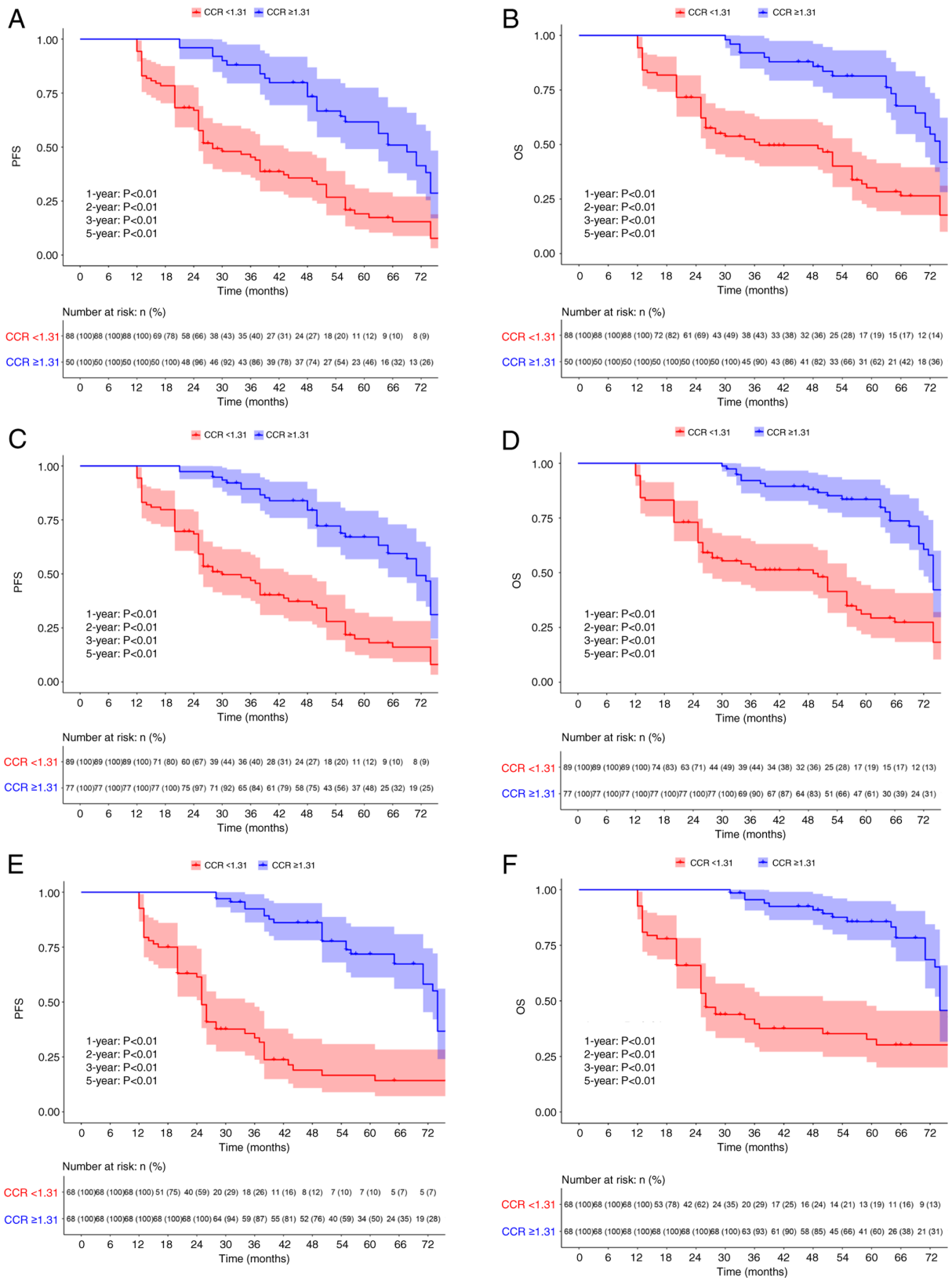

Figure 5. Kaplan-Meier survival curves in patients with multiple myeloma according to clinical stage. (A) PFS with R-ISS stage III; (B) OS with R-ISS stage III; (C) PFS with ISS stage III; (D) OS with ISS stage III; (E) PFS with DS stage III; (F) OS with DS stage III. CCR, creatinine-cystatin C ratio; OS, overall survival; PFS, progression-free survival.

the prediction of death using the CCR was 0.79 (95% CI, 0.73-0.85), which aligns with the results of the present study. The 2- and 3-year AUC values for CCR prediction of prognosis in the current study were 0.764 and 0.746, respectively, which were higher than the 1-year value of 0.712, indicating that the CCR had a greater long-term predictive value.

Clinical stage is an important factor for assessing the prognosis in patients with cancer. However, even at the same clinical stage, patient prognoses can vary (26). The present study revealed significant differences in distributions of the CCR between DS, ISS and R-ISS stages I-II and III. These findings further confirmed that the CCR reflected the tumor burden in patients with multiple myeloma and RI. Kos *et al* (25) and Kwon *et al* (32) suggested that the association between the CCR and outcome may be because CysC may reflect the tumor burden, which is similar to the findings of the present study, which revealed that the higher the clinical stage, the higher the likelihood of a lower CCR at diagnosis. CCR in each clinical staging group differed significantly. When the CCR value is delimited by 1.31 as the categorical variable, there was no statistical difference between DS stage and CCR level. Although Zhang *et al* (26) demonstrated that CysC levels notably differed between DS stages, to the best of our knowledge, no relevant clinical studies have shown the association between the CCR and DS stage. As the present study was a single-center study, verification of these results is needed. Only in the ISS and R-ISS subgroups can CCR levels be used to predict the prognosis of patients with multiple myeloma with RI. This suggests that serum CCR levels may predict the prognosis and be used to evaluate the condition in patients with multiple myeloma according to the ISS and R-ISS stage. Overall, the CCR may be considered a universally applicable, readily available and effective method for predicting the risk of adverse outcomes in patients with multiple myeloma and RI.

The present study has certain limitations. Certain patients owing to technical or financial limitations, did not undergo cytogenetic testing or FISH at the time of initial diagnosis. Therefore, it was not possible to assess the relationship between the CCR and cytogenetics. Future research should perform cytogenetics or FISH analysis to evaluate their association with CCR. The present study was a single-center retrospective study with a small sample size and potential patient selection bias. Patient nutritional status was not considered. As patients with cancer are often malnourished (29), sCr levels may be affected by nutritional status and further assessment of nutrition-related factors, such as weight loss, could elucidate the relationship between the CCR and prognosis in patients with multiple myeloma and RI. As only single-center serum data were collected in the present study, it was not possible to assess the effect of changes in the CCR on patient prognosis and survival. More real-time data should be collected through prospective studies to evaluate whether the CCR can be used to predict prognosis in patients with multiple myeloma and RI.

In conclusion, CCR may be an effective prognostic indicator for predicting the PFS and OS in patients with multiple myeloma and RI, which is helpful for more detailed prognostic stratification during clinical staging in these patients.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YS, JZ and JD analyzed data, designed and performed experiments and wrote the manuscript. WZ, YL and FD contributed to the conceptualization, data curation, formal analysis, investigation, methodology, supervision, writing of the original draft, and the review and editing of the manuscript. YS and WZ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated with Shandong First Medical University (Jinan, China) (NO.SWYX2023-582). As the study was performed by collecting retrospective anonymized patient data from electronic medical records with no influence on patient treatment, the committee waived the requirement for informed consent. Patient information was kept confidential and the principles of the Declaration of Helsinki were adhered to.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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