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ABOUT COVER

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AIMS AND SCOPE

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ORIGINAL ARTICLE

Case Control Study

Reduction rate of monoclonal protein as a useful prognostic factor in standard-risk group of newly diagnosed multiple myeloma

Min Liu, Jun-Yu Zhang

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Abstract

BACKGROUND

Multiple myeloma (MM) is a common hematologic malignancy that originates from a malignant clone of plasma cells. Solitary plasmacytoma, history of diabetes, and platelet count are considered as prognostic factors for MM. But some patients are still associated with much worse outcomes without any prognostic predictors. This study aimed to observe the reduction rate of monoclonal protein (M protein) after the first and fourth chemotherapy cycles, which is considered as a new prognostic factor for progression-free survival (PFS) in standard-risk group of newly diagnosed MM patients.

AIM

To investigate the reduction rate of M protein after first and fourth cycle chemotherapy as a useful prognostic factor.

METHODS

A total of 316 patients diagnosed with MM for the first time between 2010 and 2019 at the Lishui Municipal Central Hospital were included. All patients were diagnosed according to the National Comprehensive Cancer Network (NCCN) 2020.V1 diagnostic criteria. The risk assessment was performed by the Mayo Stratification for Macroglobulinemia and Risk-Adapted Therapy guidelines. After diagnosis, 164 patients were evaluated and underwent treatment with four to eight courses of continuous induction chemotherapy. The patients with no response after induction treatment were administered additional therapy following the NCCN 2020.V1 criteria. The following baseline data from the patients were collected: Gender, age at diagnosis, Durie-Salmon stage, glutamic-pyruvic transaminase, glutamic-oxaloacetic transaminase, catabolite activator protein, albumin/globulin ratio, lactate dehydrogenase, translocation (t)(6;14), t(11;14), maintenance regimen, total cholesterol (TC), triglyceride, and phosphorous. All baseline data and the reduction rate of M protein after each

chemotherapy cycle from the first to fourth were assessed by univariate analysis. The factors influencing the overall survival and PFS were then assessed by multivariate analysis. We found the first cycle (C1) reduction rate and the fourth cycle (C4) reduction rate as predictors of PFS. Then, PFS was compared between patients with a C1 reduction rate of M protein of ≥ 25% *vs* < 25% and ≥ 50% *vs* < 50%, and between patients with a C4 reduction rate of ≥ 25% *vs* < 25%, ≥ 50% *vs* < 50%, and ≥ 75% *vs* < 75%.

RESULTS

Multivariate analysis revealed age [hazard ratio (HR): 1.059, 95% confidence interval (95%CI): 1.033-1.085, $P \leq 0.001$], International Staging System stage (HR: 2.136, 95%CI: 1.500-3.041, $P \leq 0.001$), autotransplantion (HR: 0.201, 95%CI: 0.069-0.583, $P = 0.019$), TC (HR: 0.689, 95%CI: 0.533-0.891, $P = 0.019$), C1 reduction rate (HR: 0474, 95%CI: 0.293-0.767, $P = 0.019$), and C4 reduction rate (HR: 0.254, 95%CI: 0.139-0.463, $P = 0.019$) as predictors of PFS. The Kaplan-Meier survival analysis and the log-rank tests revealed that a higher reduction rate of M protein after first cycle (≥ 50%) and fourth cycle (≥ 75%) chemotherapy was associated with a longer PFS than the lower one.

CONCLUSION

Higher reduction rates of M protein after the first and fourth chemotherapy cycles can act as advantageous prognostic factors for PFS in standard-risk group of MM patients during initial diagnosis.

Key Words: Multiple myeloma; Monoclonal protein; Progression-free survival; Chemotherapy

Core Tip: Multiple myeloma (MM) is a common hematologic malignancy that originates from a malignant clone of plasma cells. Solitary plasmacytoma, history of diabetes, and platelet count are considered as prognostic factors for MM. But some patients are still associated with much worse outcomes without any prognostic predictors. This study aimed to observe the reduction rate of monoclonal protein after the first and fourth chemotherapy cycles, which is considered as a new prognostic factor for progression-free survival in standard-risk group of newly diagnosed MM patients.

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INTRODUCTION

Multiple myeloma (MM) is the second common hematologic malignancy that originates from B cells, and accounted for approximately 1.8% of all malignancies and led to the death of 30000 patients in 2018[1]. MM can cause kidney injury, anemia, lytic bone disease, hypercalcemia, abnormal functioning of blood coagulation, and damage of other organs[2]. Bone pain is the most common symptom that significantly impairs the quality of life in approximately 60% of patients[3]. Over the past decade, many studies have revealed nonoverlapping and overlapping genetic abnormalities in the myeloma cells and also demonstrated their impact on patient outcomes[4,5]. Del17p, translocation (t)(4;14), t(14;16), and t(14; 20) were considered as predictors of significantly shortened survival in patients with newly diagnosed MM[6-9]. In addition, according to geriatric assessment[10], due to the absence of high-risk cytogenetic abnormalities[11], both the International Staging System (ISS) and the Revised-ISS (R-ISS) were used as prognostic factors for the overall survival (OS) and progression-free survival (PFS) in patients. And ISS 1 and R-ISS 1 patients had a significantly longer PFS and OS [12], while conventional factors such as age below 80 years, beta-2-microglobulin levels, normal hemoglobin, and normal lactate dehydrogenase (LDH) levels were identified as predictors of PFS and OS[13,14]. However, the median survival of patients with MM showed great improvement after undergoing chemotherapy, which consists of proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies[15], while few patients without these predictors still demonstrated poorer outcomes. Our research revealed that the reduction rate of monoclonal protein (M protein) after the first and fourth chemotherapy cycles could act as a new advantageous prognostic factor for PFS in standard-risk group of MM patients during initial diagnosis.

MATERIALS AND METHODS

A total of 316 patients diagnosed with MM for the first time between 2010 and 2019 at the Lishui Municipal Central Hospital were included. All patients were diagnosed according to the National Comprehensive Cancer Network (NCCN) 2020.V1 diagnostic criteria. The risk assessment was performed by the Mayo Stratification of Myeloma and Risk-adapted

Therapy guidelines. After diagnosis, 164 patients were evaluated and underwent treatment with four to eight cycles of continuous induction chemotherapy. The patients with no response after induction treatment were administered additional therapy following the NCCN 2020.V1 criteria. The following baseline data from the patients were collected: Gender, age at diagnosis, Durie-Salmon (DS) stage, glutamic-pyruvic transaminase (GPT), glutamic-oxaloacetic transaminase (GOT), catabolite activator protein (CRP), albumin/globulin ratio, LDH, t(6;14), t(11;14), maintenance regimen, total cholesterol (TC), triglyceride (TG), and phosphorous (P). All baseline data and the reduction rate of M protein after each chemotherapy cycle from the first to the fourth were assessed by univariate analysis. The factors influencing the OS and PFS were then assessed by multivariate analysis. We found the first cycle (C1) reduction rate and the fourth cycle (C4) reduction rate as predictors of PFS. Then, PFS was compared between patients with a C1 reduction rate of M protein of ≥ 25% *vs* < 25% and ≥ 50% and < 50%, and betweeb patients with a C4 reduction rate of ≥ 25% *vs* < 25%, ≥ 50% *vs* < 50%, and ≥ 75% *vs* < 75%.

RESULTS

Patient characteristics

We retrospectively analyzed data from a total of 164 patients in this study, and all patients underwent treatment with four to eight cycles of continuous induction chemotherapy. The median observation time was 48.4 mo (range, 9-114 mo). The baseline characteristics for 164 MM patients diagnosed for the first time based on the reduction rate of M protein after first and fourth chemotherapy cycles are presented in Table 1. There were no significant differences in gender, DS stage, GPT, GOT, CRP, LDH, t(6;14), t(11;14), maintenance regimen, TC, TG, and P concentrations between the groups with different reduction rates of M protein after the first and fourth chemotherapy cycles (Table 1).

Prognostic impact of reduction rate of M protein after first and fourth cycle chemotherapy for standard-risk group of newly diagnosed MM

Table 2 shows the results of the univariate analysis of the factors influencing the OS and PFS. Multivariate analysis revealed age [hazard ratio (HR): 1.059, 95% confidence interval (95%CI): 1.033-1.085, $P \leq 0.001$], ISS stage (HR: 2.136, 95%CI: 1.500-3.041, $P \leq 0.001$), autotransplantion (HR: 0.201, 95%CI: 0.069-0.583, $P = 0.019$), TC (HR: 0.689, 95%CI: 0.533-0.891, $P = 0.019$), C1 reduction rate (HR: 0474, 95%CI: 0.293-0.767, $P = 0.019$), and C4 reduction rate (HR: 0.254, 95%CI: 0.139-0.463, $P = 0.019$) as predictors of PFS (Table 3).

The Kaplan-Meier survive analysis and the log-rank tests revealed that there was no difference in PFS between patients with a C1 reduction rate of M protein of ≥ 25% *vs* < 25% ($P = 0.319$), but there was a significant difference between patients with a C1 reduction rate of M protein of ≥ 50% *vs* < 50% ($P \leq 0.001$) (Figure 1). PFS did not differ significantly between patients with a C4 reduction rate of M protein of ≥ 25% *vs* < 25% ($P = 0.248$) and ≥ 50% *vs* < 50% ($P = 0.228$), but it had a significant difference between patients with a C4 reduction rate of ≥ 75% *vs* < 75% ($P \leq 0.001$) (Figure 2).

Age (HR: 1.054, 95%CI: 1.027-1.081, $P = 0.024$), ISS stage (HR: 1.879, 95%CI: 1.315-2.686, $P = 0.001$), platelet count (HR: 2.929, 95%CI: 1.269-6.756, $P = 0.012$), autotransplantion (HR: 0.211, 95%CI: 0.069-0.647, $P = 0.006$), and TC (HR: 0.735, 95%CI: 0.573-0.943, $P = 0.016$) were identified as predictors of OS (Table 4).

DISCUSSION

MM is a heterogeneous disease with adverse clinical course, and is characterized by uncontrolled proliferation and accumulation of plasma cells in the bone marrow, which is usually connected with the production of M protein and the differences in the effectiveness of therapeutic strategies and the ability to develop chemoresistance. Risk stratification factors can assist in creating a personalized therapy, thereby improving the treatment outcomes. Prognostic markers such as cytogenetics, molecular biology, and ISS stage showed an association with OS and PFS in MM patients[16]. But there are still many patients with much worse outcomes without any prognostic markers. This study aimed to find more prognostic markers that might help doctors to adjust the therapeutic strategies in time.

M protein refers to monoclonal immunoglobulins or fragments created by abnormal monoclonal B cells or plasma cells to define ISS stage in MM[12]. Its deposition could cause destruction of organs such as the kidneys and skin[17]. The M protein level as a clonal burden is considered to be helpful in predicting the risk of progression of monoclonal gammopathy of undetermined significance (MGUS) to symptomatic diseases[18]. Furthermore, monoclonal gammopathy could affect bone marrow microenvironment, resulting in increased risk of infections, osteoporosis, venous and arterial thrombosis, and bone fractures[18]. In addition, the production of M protein that has autoantibody activity or its deposition in tissues are considered responsible for severe organ damage[18]. González-Calle *et al*[19] have found Bence-Jones proteinuria as a kind of M protein disorder, and it can act as a tumor burden marker, showing a significant association with the risk of progression to symptomatic progression. Caers *et al*[20] demonstrated M protein as a significant risk factor in most of the patients with Smoldering MM (SMM) evolving into MM. Another study from Spain revealed that M protein with an increase of ≥ 10% in the first 12 mo of diagnosis was associated with progression to symptomatic MM in 71% of cases at 3 years with a median period of 1.1 year[21]. Gassiot *et al*[22] found that in patients presenting both a prior MGUS/SMM and partial remission (PR) (PR was defined as a ≥ 90% reduction of urinary M protein in 24 h or < 200 mg per 24 h and a reduction of ≥ 50% of serum M protein) after the first cycle of therapy, the PFS and OS showed significant differences from those of the remaining patients. Another study revealing that a fast response

Table 1 Baseline characteristics of multiple myeloma patients with a reduction rate of monoclonal protein after first and fourth cycles of chemotherapy

Characteristic	C1 reduction rate		*P* value	C4 reduction rate		*P* value
	< 50	≥ 50		< 75	≥ 75	
Age (yr)			≤ 0.001			0.003
< 65	25	56		21	60	
≥ 65	49	34		40	43	
Gender			0.912			0.903
Male	36	43		37	42	
Female	38	47		39	46	
ISS stage			≤ 0.001			≤ 0.001
I	5	39		2	42	
II	31	34		23	42	
III	38	17		36	19	
DS stage			0.087			0.783
I	1	1		1	1	
II	7	20		9	19	
III	66	70		51	83	
GPT			0.657			0.985
≤ 40	71	85		58	98	
> 40	3	5		3	5	
GOT			0.510			0.617
≤ 40	67	84		57	94	
> 40	7	6		4	9	
CRP			0.704			0.880
≤ 10	53	62		42	83	
> 10	21	28		19	20	
A/G			0.916			0.041
≤ 0.5	29	36		18	47	
> 0.5	45	54		43	56	
LDH			0.215			0.530
≤ 245	54	73		46	82	
> 245	20	17		15	21	
t(6;14)	3	3	1.000	2	4	0.405
t(11;14)	2	2	1.000	1	3	0.615
Platelet count			≤ 0.001			≤ 0.001
≥ 100	55	88		45	98	
< 100	19	2		16	5	
Herpes	13	19	0.569	9	23	
Autotransplantation	5	20	0.006	5	20	0.020
TC (mmol/L)			0.903			0.767
< 5.2	63	76		52	86	
≥ 5.2	11	14		9	17	

TG (mmol/L)			0.546			0.778
< 1.71	51	58		41	67	
≥ 1.71	23	32		20	36	
P (mmol/L)			0.587			0.568
< 1.07	17	24		13	26	
≥ 1.07	57	66		48	77	

C1: The first cycle; C4: The fourth cycle; ISS: International Staging System; DS: Durie-Salmon; GPT: Glutamic-pyruvic transaminase; GOT: Glutamic-oxaloacetic transaminase; CRP: Catabolite activator protein; A/G: Albumin/globulin; LDH: Lactate dehydrogenase; T: Translocation; TC: Total cholesterol; TG: Triglyceride; P: Phosphorous.

Table 2 Univariate analysis of progression-free survival and overall survival

Prognostic factor	PFS		OS	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age (yr)	1.051 (1.031-1.071)	≤ 0.001	1.034 (1.012-1.055)	0.002
Gender	1.265 (0.828-1.931)	0.277	1.412 (0.926-2.152)	0.109
Classification	1.037 (0.949-1.132)	1.037	1.093 (0.999-1.196)	0.053
ISS stage	1.718 (1.247-2.366)	0.001	2.093 (1.520-2.883)	≤ 0.001
DS stage	2.094 (1.082-4.054)	0.028	1.982 (1.015-3.869)	0.045
GPT	1.011 (1.002-1.021)	0.019	1.009 (0.999-1.019)	0.082
GOT	1.022 (1.011-1.033)	≤ 0.001	1.025 (1.013-1.038)	≤ 0.001
CRP	1.002 (0.996-1.007)	0.593	1.002 (0.996-1.008)	0.491
A/G	1.041 (0.698-1.553)	0.844	1.149 (0.754-1.751)	0.518
LDH	1.003 (1.001-1.004)	≤ 0.001	1.003 (1.002-1.005)	≤ 0.001
t(6;14)	1.021 (0.319-3.266)	0.972	1.285 (0.399-4.134)	0.674
t(11;14)	1.149 (0.281-4.708)	0.847	1.188 (0.290-4.871)	0.811
Platelet count	9.604 (4.965-18.578)	≤ 0.001	8.437 (4.528-15.721)	≤ 0.001
Herpes	0.821 (0.451-1.495)	0.52	0.908 (0.498-1.653)	0.751
Chemotherapy regimen	1.005 (0.856-1.180)	0.952	0.949 (0.795-1.133)	0.564
Autotransplantation	0.339 (0.137-0.842)	0.020	0.347 (0.140-0.860)	0.022
TC	0.773 (0.631-0.947)	0.013	0.757 (0.617-0.927)	0.007
TG	0.861 (0.666-1.114)	0.255	0.846 (0.642-1.113)	0.232
P	1.143 (0.953-1.370)	0.15	1.113 (0.934-1.325)	0.232
C1 reduction rate	0.412 (0.325-0.521)	≤ 0.001	0.438 (0.346-0.554)	≤ 0.001
C2 reduction rate	0.412 (0.325-0.523)	≤ 0.001	0.441 (0.351-0.553)	≤ 0.001
C3 reduction rate	0.390 (0.303-0.501)	≤ 0.001	0.377 (0.290-0.490)	≤ 0.001
C4 reduction rate	0.358 (0.283-0.455)	≤ 0.001	0.345 (0.267-0.445)	≤ 0.001

PFS: Progression-free survival; OS: Overall survival; HR: Hazard Ratio; 95%CI: 95% confidence interval; ISS: International Staging System; DS: Durie-Salmon; GPT: Glutamic-pyruvic transaminase; GOT: Glutamic-oxaloacetic transaminase; CRP: Catabolite activator protein; A/G: Albumin/globulin; LDH: Lactate dehydrogenase; T: translocation; TC: Total cholesterol; TG: Triglyceride; P: Phosphorous; C1: The first cycle; C2: The second cycle; C3: The third cycle; C4: The fourth cycle.

to the first treatment cycle in MM patients is the major predictor of long-term response to lenalidomide and dexamethasone therapy also supported the same concept[22]. Atkin *et al*[23] believed that M protein production is reduced by treatment with chemotherapy, which improved the outcomes of MGUS.

Table 3 Multivariate analysis of progression-free survival

Prognostic factor	HR (95%CI)	*P* value
Age	1.059 (1.033-1.085)	≤ 0.001
ISS stage	2.136 (1.500-3.041)	≤ 0.001
DS stage	1.622 (0.264-1.622)	0.264
GPT	1.017 (0.997-1.036)	0.097
GOT	1.002 (0.977-1.028)	0.857
LDH	1.000 (0.997-1.003)	0.944
Platelet count	1.880 (0.732-4.830)	0.189
Maintenance regimen	0.410 (0.236-0.710)	0.001
Autotransplantation	0.201 (0.069-0.583)	0.003
TC	0.689 (0.533-0.891)	0.005
C1 reduction rate	0.474 (0.293-0.767)	0.002
C2 reduction rate	0.792 (0.440-1.427)	0.438
C3 reduction rate	1.974 (0.921-4.230)	0.08
C4 reduction rate	0.254 (0.139-0.463)	≤ 0.001

HR: Hazard ratio; 95%CI: 95% confidence interval; ISS: International Staging System; DS: Durie-Salmon; GPT: Glutamic-pyruvic transaminase; GOT: Glutamic-oxaloacetic transaminase; LDH: Lactate dehydrogenase; TC: Total cholesterol; C1: The first cycle; C2: The second cycle; C3: The third cycle; C4: The fourth cycle.

Table 4 Multivariate analysis of overall survival

Prognostic factor	HR (95%CI)	*P* value
ISS stage	1.879 (1.315-2.686)	0.001
Age	1.054 (1.027-1.081)	0.024
DS stage	1.829 (0.791-4.233)	0.158
GOT	1.009 (0.988-1.031)	0.395
LDH	0.998 (0.996-1.001)	0.264
Platelet count	2.929 (1.269-6.756)	0.012
Autotransplantation	0.211 (0.069-0.647)	0.006
TC	0.735 (0.573-0.943)	0.016
C1 reduction rate	0.868 (0.543-1.387)	0.553
C2 reduction rate	0.680 (0.386-1.197)	0.181
C3 reduction rate	1.055 (0.592-1.879)	0.856
C4 reduction rate	0.608 (0.350-1.058)	

HR: Hazard ratio; 95%CI: 95% confidence interval; ISS: International Staging System; DS: Durie-Salmon; GOT: Glutamic-oxaloacetic transaminase; LDH: Lactate dehydrogenase; TC: Total cholesterol; C1: The first cycle; C2: The second cycle; C3: The third cycle; C4: The fourth cycle.

In this retrospective analysis, we found a significant difference in the outcomes between a standard-risk group of newly diagnosed MM patients with a C1 reduction rate of M protein of ≥ 50% *vs* < 50%, and between those with a C4 reduction rate of M protein of ≥ 75% *vs* < 75%; the median PFS was 20 mo *vs* 33 mo and 18 mo *vs* 30 mo, respectively, showing a significant difference between groups. In multivariate analysis, a higher reduction rate of M protein after the first and fourth chemotherapy cycles was demonstrated to be advantageous factors for PFS, with the reduction rate of M protein after the fourth chemotherapy cycle of ≥ 75% being stronger. Although the reduction rate of M protein after the first and fourth chemotherapy cycles were not identified as independent prognostic factors for OS in multivariate analysis, there is a trend of a longer OS associated with a higher reduction rate of M protein after the fourth chemotherapy cycle (≥ 75%). It has been more than 30 years since chemotherapy was initially combined with autologous

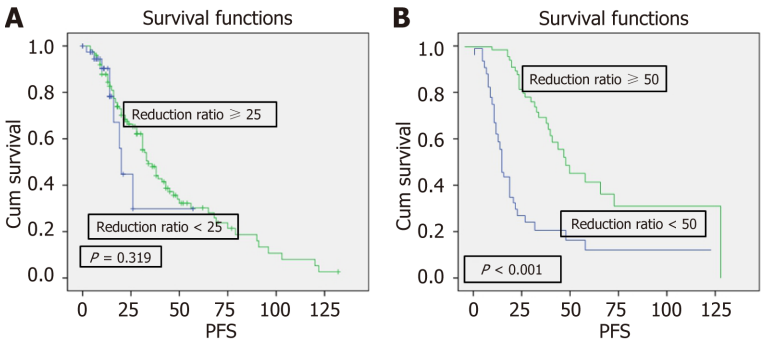

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Figure 1 Kaplan-Meier analysis of progression-free survival of patients with different reduction rates of monoclonal protein after the first cycle of chemotherapy (*P* < 0.001). A: Progression-free survival (PFS) of patients with a reduction rate of monoclonal protein (M protein) after first chemotherapy of ≥ 25% *vs* < 25%; B: PFS of patients with a reduction rate of M protein after first chemotherapy of ≥ 50% *vs* < 50%. PFS: Progression-free survival.

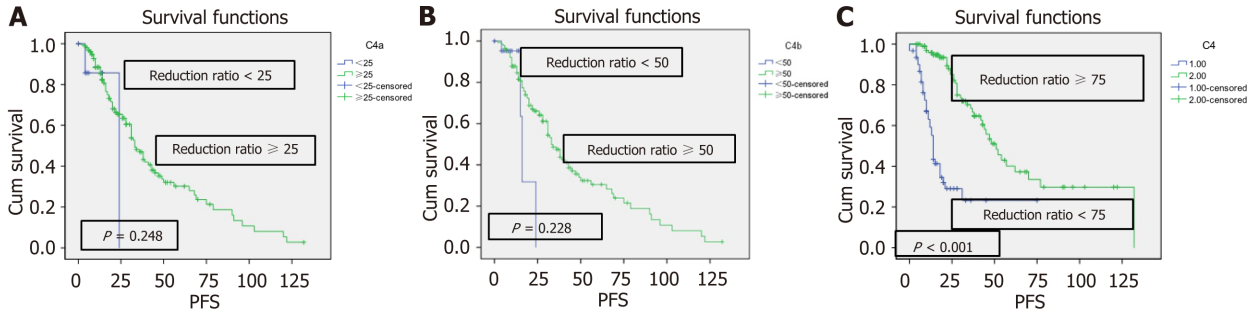

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Figure 2 Kaplan-Meier analysis of progression-free survival of patients with different reduction rates of monoclonal protein after the fourth cycle of chemotherapy (*P* < 0.001). A: Progression-free survival (PFS) of patients with a reduction rate of monoclonal protein (M protein) after the fourth chemotherapy cycle of ≥ 25% *vs* < 25%; B: PFS of patients with a reduction rate of M protein after fourth chemotherapy of ≥ 50% *vs* < 50%; C: PFS of patients with a reduction rate of M protein after fourth chemotherapy of ≥ 75% *vs* < 75%. PFS: Progression-free survival.

stem cell transplantation (ASCT) for the treatment of MM, which remained to be standard care for few patients with newly diagnosed MM[24-26]. Our study also supported this, and ASCT after chemotherapy was regarded as a protective factor for both PFS and OS. This might be one of the reasons for the association of a higher reduction rate of M protein with a longer PFS. After achieving a high reduction rate, more patients will have a chance to undergo ASCT. Furthermore, our study found TC as a protective factor for both PFS and OS. Jafri *et al*[27] revealed an inverse correlation between cholesterol level and the risk of hematologic malignancy, but the mechanism remains unclear. A previous study revealed that low platelet count is associated with an unfavorable OS[28]. Similar to previous studies, high ISS stage and age were identified as disadvantageous factors for PFS and OS in this study[29-31].

CONCLUSION

Our study have identified new independent prognostic factors for patients with newly diagnosed MM, and a higher reduction rate of M protein after the first chemotherapy cycle (≥ 50%) and the fourth chemotherapy cycle (≥ 75%) is associated with a longer PFS. The high reduction rate of M protein after the fourth chemotherapy cycle is associated with OS. To our knowledge, this is the first study to analyze the effects of the reduction rate of M protein after chemotherapy in MM patients. The new prognostic factors could help doctors to administer the treatment in time.

ARTICLE HIGHLIGHTS

Research background

Multiple myeloma (MM) is a common hematologic malignancy that originates from a malignant clone of plasma cells. Solitary plasmacytoma, history of diabetes, and platelet count are considered as prognostic factors for MM. But some patients are still associated with much worse outcomes without any prognostic factors.

Research motivation
To study the potential prognostic factors in MM patients.

Research objectives
This study aimed to observe the reduction rate of monoclonal protein (M protein) after the first and fourth chemotherapy cycles, which is considered as a new prognostic factor for progression-free survival (PFS) in standard-risk group of newly diagnosed MM patients.

Research methods
We retrospectively analyzed 164 patients diagnosed with standard-risk MM for the first time, and compared the PFS and overall survival (OS) between patients with a reduction rate of M protein after first chemotherapy of ≥ 50% *vs* < 50% and between patients with a reduction rate of M protein after the fourth chemotherapy cycle of ≥ 75% *vs* < 75%.

Research results
Multivariate analysis revealed age [hazard ratio (HR): 1.059, 95% confidence intervals (95%CI): 1.033-1.085, $P \leq 0.001$], International Staging System stage (HR: 2.136, 95%CI: 1.500-3.041, $P \leq 0.001$), autotransplantion (HR: 0.201, 95%CI: 0.069-0.583, $P = 0.019$), total cholesterol (HR: 0.689, 95%CI: 0.533-0.891, $P = 0.019$), the first cycle reduction rate (HR: 0474, 95%CI: 0.293-0.767, $P = 0.019$), and the fourth cycle reduction rate (HR: 0.254, 95%CI: 0.139-0.463, $P = 0.019$) as predictors of PFS. The Kaplan-Meier survival analysis and the log-rank tests revealed that a higher reduction rate of M protein after the first cycle (≥ 50%) and fourth cycle (≥ 75%) chemotherapy was associated with a longer PFS than the lower one.

Research conclusions
Our study have identified new prognostic factors for patients with initially diagnosed MM, and a higher reduction rate of M protein after the first chemotherapy cycle (≥ 50%) and the fourth chemotherapy cycle (≥ 75%) is associated with a longer PFS. The high reduction rate of M protein after the fourth chemotherapy cycle could is associated with the OS.

Research perspectives
To our knowledge, this is the first study to analyze the effects of the reduction rate of M protein after chemotherapy in MM patients. The new prognostic factors could help doctors to administer the treatment in time.

FOOTNOTES

Author contributions: Zhang JY and Liu M contributed equally to this work; Zhang JY designed the research study; Liu M performed the research; Zhang JY and Liu M analyzed the data and wrote the manuscript; all authors have read and approved the final manuscript.

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