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THE RELATIONSHIP BETWEEN PROGNOSTIC FACTORS AND TREATMENT OUTCOME OF MULTIPLE MYELOMA

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ABSTRACT

Objectives: To analyze the relationship between prognostic factors to outcomes of number of multiple myeloma (MM) treatment regimens at Ho Chi Minh city (HCMC) Blood Transfusion and Hematology Hospital from 2018 to 2021.

Subjects and methods: A descriptive and analytical study on 111 patients newly diagnosed with MM from January 2018 to December 2021 according to IMWG 2014 standards who came for examination and treatment at HCMC Blood Transfusion and Hematology Hospital.

Results: The prognostic factors associated with statistical significance to the rate of at least very good partial response (VGPR) compared with the other group including: Clinical index ECOG < 2, NLR < 2.25, platelet ≥ 150, novel treatment regimen and myeloma prognostic index (MPI).

Conclusion: Clinical index ECOG < 2, NLR < 2.25, platelet ≥ 150, new treatment regimen and MPI were the prognostic factors associated with MM.

Keywords: Multiple myeloma, prognostic factors, relationship.

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1. INTRODUCTION

Pathology of MM is a complex process that leads to the multiplication of a malignant cell line from bone marrow. The most widely supported hypothesis is that MM develops from monoclonal gammopathy of undetermined significance (MGUS) [1]. Malignant plasma cell proliferation affects the normal development of blood cell lines (erythrocytes, leukocytes, and platelets). Destruction of bone marrow structure leads to complications such as osteoporosis, fractures, hypercalcemia and kidney failure...[2]. A good understanding of the prognostic factors associated with MM is crucial in the treatment strategy. So we conducted this study with the aim of analyze the relationship between prognostic factors to outcomes of some MM treatment regimens at HCMC Blood Transfusion and Hematology Hospital from 2018 to 2021.

2. RESEARCH SUBJECTS AND METHODS

2.1. Patient population

111 patients newly diagnosed with MM from January 2018 to December 2021 according to IMWG 2014 standards who came for examination and treatment at HCMC Blood Transfusion and Hematology Hospital.

* Exclusion criteria: Patients who refused to participate in the study; patients was diagnosed at the HCMC Blood Transfusion and Hematology Hospital but did not adhere to treatment, gave up treatment or transferred to another medical facility, so the necessary information was not recorded.

2.2. Research methods

***Study design*:** Descriptive and analytical study

Research variables:

The relationship between genetic markers (R-ISS and Mayo-clinic), clinical factors (age, ECOG), hematologic factors (bone marrow plasma-cell percentage, Hb, NLR and SLTC), biochemical factors (creatinine, calcium levls, β2M, albumin, LDH, FLCr) and the rate of VGPR.

Relationship between response to treatment regimens (novel regimens and classic regimens): Classic regimens using corticosteroids (Methylprednisolon, Dexamethasone), Melphalan, Cyclophosphamide, Doxorubicin, Vincristine,… such as VAD (Vincristin, Adriamicin, Dexamethasone), MP (Melphalan, Prednisolone) and MPT (Melphalan, Prednisolone, Thalidomide); novel regimens including LD (Lenalidomide, Dexamethasone), VRD (Bortezomib, Lenalidomide, Dexamethasone), VTD (Bortezomib, Thalidomide, Dexamethasone), VCD (Bortezomib, Cyclophosphamide, Dexamethasone), VD (Bortezomib, Dexamethasone).

2.3. Statistical analysis: Data were entered and analyzed using IBM SPSS software version 22.0.

3. RESULTS

Table 1. Treatment response rate according to genetic abnormalities

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
Mayo stratification	Standard risk	12	70.59	5	29.41	> 0.05
	Intermediate risk	3	60	2	40	
	High risk	3	75	1	25	
R-ISS classification	R-ISS I	3	75	1	25	> 0.05
	R-ISS II	12	63.16	7	36.84	
	R-ISS III	3	75	1	25	

VGPR - Very Good Partial Response

According to the Mayo stratification: Achivement rates of at least VGPR in high, intermediate and standard risk groups were 75%, 60% and 70.59%, respectively. There was no relationship between genetic abnormalities and response to treatment (p>0,05).

According to the R-ISS classification: Achivement rates of at least VGPR in high, intermediate and standard risk groups were 75%, 63.16% and 75%. There was no relationship between genetic abnormalities and response to treatment (p>0,05).

Table 2. The relationship between age and treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
Age (year)	< 65	35	47.30	39	52.70	> 0.05
	≥ 65	16	43.24	21	56.76	

There was no statistically significant relationship between age and treatment response in this study (p>0.05).

Table 3. The relationship between clinical factors and treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
ECOG	< 2 point	22	78.57	6	21.43	<0.01
	≥ 2 point	29	34.94	54	65.06	

The achivement rates of at least in VGPR between ECOG < 2 group and ECOG ≥ 2 group were 78.57% and 34.94%, respectively. Standard-risk group had a higher achivement rate of at least VGPR than high-risk group (p <0.01).

Table 4. Univariate analysis of hematological factors to treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
Bone marrow plasma-cell percentage	< 30%	30	50	30	50	> 0.05
	≥ 30%	21	41.18	30	58.82	
Hb	≥ 100 g/L	17	54.84	14	45.16	> 0.05
	< 100 g/L	34	42.50	46	57.50	
NLR	< 2.25	35	55.56	28	44.44	< 0.05
	≥ 2.25	16	33.33	32	66.67	
Platelet	< 150 G/L	9	30	21	7	< 0.05
	≥ 150 G/L	42	51.85	39	48.15	

Rates of achieving at least VGPR in NLR < 2.25 and NLR ≥ 2.25 groups were 55.56% and 33.33%, respectively (p< 0.05).

Rates of achieving at least VGPR in platelet < 150 G/L and ≥ 150 G/L groups were 30% and 51.85%, respectively (p< 0.05).

Table 5. Univariate analysis of biochemical factors to treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
Albumin	< 35 g/L	30	45.45	36	54.55	> 0.05
	≥ 35 g/L	21	46.67	24	53.33	
β2M	< 5.5 mg/L	22	57.89	16	42.11	> 0.05
	≥ 5.5 mg/L	29	39.73	44	60.27	
Creatinin	< 177 µmol/L	36	48.65	38	51.35	> 0.05
	≥ 177 µmol/L	15	40.54	22	59.46	
FLCr (n=74)	< 100 and > 0.01	18	39.13	28	60.87	> 0.05
	≥ 100 or ≤ 0.01	11	39.29	17	60.71	
Calci (n=106)	< 2.67 mmol/L	39	46.43	45	53.57	> 0.05
	≥ 2.67 mmol/L	9	40.91	13	59.09	

There was no statistically significant relationship between treatment response and biochemical prognostic factors.

Table 6. The relationship between treatment regimens and treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
Treatment regimen	Novel regimen	31	62	19	38	<0.01
	Classic regimen	20	32.79	41	67.21	

Rates of achieving at least VGPR in novel and classic treatment groups were 62% and 32.79% respectively. The difference was statistically significant (p <0.01).

Table 7. Relationship between MPI categories and treatment response

Factor	Category	At least VGPR		The others		p
		n	%	n	%	
MPI	Standard risk	12	80	3	20	<0.01
	Intermediate risk	14	53.85	12	46.15	
	High risk	25	35.71	45	64.29	

Grouping according to MPI, rates of achieving at least VGPR gradually decreased in standard, intermediate and high risk patients were 80%, 53.85% and 35.71%, respectively (p <0.01).

Table 8. Multivariate analysis of prognostic factors to treatment response

Factor	Category	Risk of not achieving at least VGPR		
		HR	95% CI	p
ECOG	< 2 point	1	1.01 - 5.66	0.05
	≥ 2 point	2.39		
NLR	< 2.25	1	0.94 - 2.78	0.08
	≥ 2.25	1.62		
SLTC	< 150 G/L	1.48	0.85 - 2.57	0.17
	≥ 150 G/L	1		
Regimen	Classic	1	0.33 - 1.00	0.05
	Novel	0.57		

Multivariate analysis showed that only ECOG and treatment regimen had a statistically significant effect on treatment response. ECOG ≥ 2 points increased 2.39 times risk of not achieving at least VGPR. Novel regimen reduced the risk of achieving not at least VGPR by 0.57 times compared with classic regimen.

4. DISCUSSION

Grouping according to Mayo stratification: Achivement rates of at least VGPR in high, intermediate and standard risk groups were 75%, 60% and 70.59%, respectively. Tandon N et al. evaluated after 2 courses of treatment in a group of 840 newly diagnosed patients with MM, showing that achivement rates of at least VGPR in high-risk groups was 28% [3].

In our study, achivement rates of at least VGPR were 47.30% in <65 age group and 43.24% in ≥65 age group. In the study by Tandon N. et al., achivement rates of at least VGPR in patients aged ≥70 was 25% [3]. The rate of of at least VGPR was higher in the younger group, but the difference in our study was not significant.

Achivement rates of at least VGPR in ECOG < 2 group and ECOG ≥ 2 group were 78.57% and 34.94%, respectively. Research on the relationship between ECOG and treatment response is relatively limited. Our research results are similar to those of authors NJ Bahlis et al. (79% and 21%) [4].

Achivement rate of at least VGPR in group with plasma-cell percentage ≥30% (41.18%) was significantly lower than group with plasma-cell percentage <30% (50%). According to Tandon N et al., achivement rate of at least VGPR in group with plasma-cell percentage ≥ 50% was 56% [3]. In our study, low plasma-cell percentage group had a better treatment response than high plasma-cell percentage group with the same treatment regimen.

Achivement rate of at least VGPR in group with Hb ≥ 100 g/L (54.84%) was higher than group with Hb < 100 g/L (42.50%). However, the difference was not statistically significant. In the study by Tandon N et al., achivement rate of at least VGPR in group with Hb < 100 g/L was 36% [3]. In our study, achivement rate of at least VGPR in group with NLR < 2.25 (55.56%) was significantly higher than group with NLR ≥ 2.25 (33.33%), p value < 0.05. Many recent studies have shown that NLR is a prognostic factor for hematopoietic cancers, including MM [5], [6].

Achivement rate of at least VGPR in platelet ≥150 G/L group (51,85%) was significantly higher than platelet <150 G/L group (30%), p value < 0.05. In the study by Bakeer M et al., achivement rate of at least VGPR in low platelet group (46.7%) was lower than normal platelet group (50%) [7].

Achivement rate of at least VGPR were 40.54% in creatinin ≥ 177 µmol/L group and 48.65% in creatinin < 177 µmol/L group. In the study by Tandon N et al., Achivement rate of at least VGPR in creatinin > 176.8 µmol/L group was 21% [3]. Renal failure is a complication and also a diagnostic criterion. Patients with renal impairment may have limited chemotherapy doses and optimal therapy. The ability to achieve treatment response will be reduced, leading to a decrease in the response rate compared to the other group.

Achivement rate of at least VGPR were 39.13% in FLCr < 100 and > 0.01 group and 39.29% in FLCr ≥ 100 or ≤ 0,01 group. The difference between two groups was not significant. Author Nguyen Thuy Duong evaluated treatment response of patients with

light-chain MM after 6 courses of treatment, showing that achivement rate of at least VGPR was 76.71% [8].

Achivement rate of at least VGPR were 40.91% in calci ≥ 2,67 mmol/L group and 46.43% in calci < 2,67 mmol/L group. In the study by Tandon N et al., achivement rate of at least VGPR were 10% in calci ≥ 2,67 mmol/L group [3].

Besides prognostic factors, our study also recorded relationship between treatment regimens and treatment response. Rate of at least VGPR was higher in group treated with novel regimen (62.00%) than with classic regimen (32.79%). p value <0.01. This showed the effectiveness of novel regimens including Bortezomib or Lenalidomide. In the study by Miguel JFS et al., the overall response rates of VMP group and MP group were 71% and 35% [9].

5. CONCLUSION

The prognostic factors associated with statistical significance to the rate of at least VGPR compared with the other group including: Clinical index ECOG < 2, NLR < 2.25, platelet ≥ 150, novel treatment regimen and MPI.

REFERENCES

[1] O. Landgren. R. A. Kyle. R. M. Pfeiffer. et al., Monoclonal gammopathy of undetermined significance (MGUS) consistently precedes multiple myeloma: a prospective study. Blood. 113(22): 5412-7, 2009.

[2] D. A. Goldstein, Denosumab for bone lesions in multiple myeloma - what is its value? Haematologica. 103(5): 753-754, 2018.

[3] N. Tandon. S. Sidana, Outcomes with early response to first-line treatment in patients with newly diagnosed multiple myeloma3(5): 744-750, 2019.

[4] N. J. Bahlis. A. Corso. L. O. Mugge. et al., Benefit of continuous treatment for responders with newly diagnosed multiple myeloma in the randomized FIRST trial. Leukemia. 31(11): 2435-2442, 2017.

[5] Y. Li. H. Li. W. Li. et al., Pretreatment neutrophil/lymphocyte ratio but not platelet/lymphocyte ratio has a prognostic impact in multiple myeloma. J Clin Lab Anal. 31(5), 2017.

[6] A. J. Templeton. M. G. McNamara. B. Seruga et al., Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 106(6): dju124, 2014.

[7] M. Bakeer. A. C. Zubair. V. Roy, Low baseline platelet count predicts poor response to plerixafor in patients with multiple myeloma undergoing autologous stem cell mobilization. Cytotherapy. 22(1): 16-20, 2020.

[8] Nguyen Thuy Duong, Study clinical features. Subclinical and treatment results in multiple light chain myeloma at the National Institute of Hematology and Blood Transfusion. Master thesis in medicine, 2018.

[9] J. F. San Miguel. R. Schlag. N. K. Khuageva et al., Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. N Engl J Med. 359(9): 906-17, 2008.