Hematopoietic Score for the Prognostic Evaluation of Multiple Myeloma Patients Undergoing First-Line Treatment With A Bortezomib-Based Regimen

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Research Article

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Abstract

Background: It is very important to evaluate the prognosis of multiple myeloma (MM) patients before starting treatment. Although hematopoietic status may have a significant impact on patient survival, it has not received sufficient attention in current clinical practice.

Methods: This was a retrospective study of 328 newly diagnosed MM patients received first-line treatment with a bortezomib-based regimen. The effects of hematopoietic factors, including hemoglobin (Hgb) levels, mean corpuscular volume (MCV), and platelet count (Plt) on the prognosis of the patients were analysed.

Results: Hgb<100 g/L, MCV>99.1fL and Plt<150×10^9/L significantly affect the progression-free survival (PFS) and overall survival (OS) of MM patients, each of the above factors was assigned a value of 1 to generate a hematopoietic score. According to the results, 93 (28.4%), 103 (31.4%), 90 (27.4%) and 42 (12.8%) patients had a score of 0, 1, 2, 3, respectively. The median PFS were 38.7, 55.9, 23.9 and 16.7 months, respectively (P<0.001), and the median OS were not reached (NR), 68.4months, 53.6 and 33.2 months, respectively (P<0.001). Multivariable analysis showed that hematopoietic score (2-3 vs 0-1, HR, 1.64) and bone marrow plasma cell percentage (>30%, HR, 1.54) are independent prognostic predictors for PFS; age (≥70 years, HR, 1.67), hematopoietic score (2-3 vs 0-1, HR, 1.60), serum creatinine level (>177umol/L, HR, 2.15) and bone marrow plasma cell percentage (>30%, HR, 1.81) are independent prognostic predictors of OS.

Conclusions: This study suggests that the hematopoietic score can be used to evaluate the prognosis of newly treated MM patients in the era of new drugs. However, there is still a need to enlarge the number of cases and carry out prospective research to validate this conclusion.

Introduction

Multiple myeloma (MM) is characterized by the clonal proliferation of malignant plasma cells, which can produce a large amount of monoclonal immunoglobulin (M protein). MM cells and their secreted M protein can cause a series of clinical symptoms, such as bone destruction, hypercalcemia, anemia, and renal insufficiency. A large number of new targeted drugs, such as proteasome inhibitors and immunomodulators, have entered clinical practice since 2000, significantly improving the efficacy of treatment for MM and increasing the median survival of patients from 3–5 years to 5–7 years (1–3). Currently, the proteasome inhibitor bortezomib and the immunoregulatory agents thalidomide and lenalidomide are the most important and commonly used drugs for the treatment of MM in China. Since February 2006, bortezomib has been used in our centers for the first-line treatment of Chinese MM patients (4–6), with an overall response rate (ORR, partial remission and better) of 90%; over 60% of patients achieve very good partial remission (VGPR) or better.

MM is a heterogeneous disease, and it is important to assess the prognosis of patients before the disease is treated. The Durie-Salmon staging system was once the most important staging system, and

included the following factors: Hgb level, serum calcium level, extent of bone lesions, M protein level, and renal function status (6). However, this staging system is closely related to the tumor burden of MM, and its prognostic significance is often questioned in the era of new drugs. Currently, the International Staging System (ISS) and the latest Revised International Staging System (R-ISS) are commonly applied in patients undergoing first-line therapy. However, the former contains only two indicators, namely, the serum albumin and β2-microglobulin levels, while the latter combines those with the serum lactate dehydrogenase (LDH) level and/or fluorescence in situ hybridization (FISH)-based cytogenetic abnormalities (7, 8), which have limited prognostic evaluation in MM patients.

Anemia is very common clinical symptom in MM patients for a variety of reasons, for example, the infiltration of plasma cells into the bone marrow inhibits erythropoiesis, and the bone marrow microenvironment is altered; there is also a decline in the level of in erythropoietin due to renal insufficiency and anemia owing to the release of various inflammatory factors that affect normal hematopoiesis. The role of Hgb in the prognosis of MM patients is clearly defined in the Durie-Salmon staging system and 100 g/L is used as one of the cut-off values for an abnormal Hgb level (6). In addition, abnormal red blood cell size, indicated by abnormal red blood cell distribution width (RDW) or average red blood cell volume values, and Plt counts are important MM prognostic indicators (2, 6, 9–13). However, these indicators have not received enough attention in current clinical practice.

Therefore, this study retrospectively analyzed the effect of the "hematopoietic score" including hemoglobin (Hgb), mean corpuscular volume (MCV) and platelet (plt) count on the prognosis of MM patients treated with bortezomib as first-line therapy, in the hope that this score could be served as an important supplement to the prognostic evaluation of newly diagnosed MM patients in the new drug era.

Methods

Patients

This study was a retrospective analysis and was approved by the Ethics Committee of the First Affiliated Hospital of the Medical School of Zhejiang University. From May 2013 to June 2019, patients who were newly diagnosed according to the World Health Organization (WHO) or International Myeloma Working Group (IMWG) diagnostic criteria in our center were included if they had symptomatic MM with detectable M protein in their blood and/or urine and received first-line treatment with bortezomib-based regimen. From the beginning of treatment to the end of follow-up, all patients were informed of their condition and survival status through inpatient services, outpatient services or telephone contact.

Treatment regimen and efficacy evaluation

All patients received a bortezomib-based regimen either as: a two-drug combined PD regimen (bortezomib combined with dexamethasone) or a three-drug combined regimen, with a third drug, such as cyclophosphamide (PCD), adriamycin (PAD) or thalidomide (PTD), added to the PD regimen. The specific administration method is detailed elsewhere (5). If indicated by the patient’s age, physical condition and

willingness and if partial remission (PR) was obtained after at least 3-4 courses of induction treatment, autologous hematopoietic stem cell transplantation (ASCT) performed. After induction therapy with or without ASCT, patients received maintenance therapy based on bortezomib, lenalidomide, or thalidomide.

The IMWG efficacy evaluation standard was used to assess the efficacy of treatment, including complete remission (CR), VGPR, PR, stable disease (SD) and progressive disease (PD) (15). Progression-free survival (PFS) was defined as the time from the beginning of the patients' first course of treatment to disease progression, death or the final follow-up visit. Overall survival (OS) was calculated from the time of the first course of treatment to death or the final follow-up visit.

Data acquisition

All patients were hospitalized during the initial diagnosis and treatment, and data regarding routine blood examinations, hepatic and renal function indicators, LDH levels, and bone marrow examination results were obtained from the hospital information system. All patients were evaluated based on the Durie-Salmon staging system and the ISS at the time of diagnosis. Using fluorescence in situ hybridization (FISH), bone marrow cells were examined for specific chromosomal abnormalities, including del-(17p13), 1q21 gain, del(13q14), and 14q32 rearrangement, and specific translocations, including t (4;14), t (11;14), and t (14;16), were detected in a small number of patients with 14q32 rearrangement. Retrospective assessment of the patients was based on the R-ISS, combining the patients' ISS stages, serum LDH levels, and FISH results, of which 1q amplification was also considered a genetic abnormality indicative of a poor prognosis (14). The data obtained included the WBC count, Hgb level, MCV, Plt count, serum creatinine level, serum LDH level, bone marrow plasma cell ratio and FISH examination results of bone marrow cells.

Statistical analysis

All patients were followed up until June 30, 2020, and the efficacy of treatment was evaluated after completing each course. The cut-off values for the Hgb level (<100 g/L); Plt count ($<150\times10^9$/L) were based on the literature (2) The upper limit of normal for the MCV in our center is 99.1fL, which was selected as the threshold. The boundary value of other data is based on the normal boundary value of our center or the ROC curve. Chi-square test was employed for comparisons of classification data, the Kaplan-Meier method was used to generate survival curves and the log-rank test was used to compare differences in patient survival. Univariate analysis using the Cox proportional hazards model was performed for age; Durie-Salmon stage; ISS, R-ISS; bone marrow plasma cell ratio; blood creatinine level; blood LDH level; peripheral blood WBC count, Hgb level, MCV, Plt count and the hematopoietic score to evaluate their impact on patient survival. All statistical tests were two-sided and P-values <0.05 were considered to be statistically significant. Only factors with P-values <0.1 were included in the multivariable analysis. The hazard ratio (HR) and 95% confidence intervals (CI) were reported. The statistical analysis was performed using SPSS for Windows 20.0.

Results

Hgb level, MCV and platelet count and patient characteristics

A total of 328 newly diagnosed MM patients were enrolled in this study, of whom 180 were males and 148 were females; the median age was 63 years (range from 31 to 84). Table 1 shows the baseline characteristics and treatment specifics of the patients. According to the results of the routine peripheral blood examinations at the time of diagnosis, 72 patients (22.0%) had WBC counts lower than normal (4×10^9/L), 197 patients (60.1%) had an Hgb level lower than 100 g/L, 84 patients (25.6%) had a MCV higher than normal (99.1fL) and 128 patients (39.0%) had a Plt count lower than 150×10^9/L.

Table 1
Baseline characteristics of all patients

Baseline characteristics	N = 328
Age(y), median, (range)	63 (31–84)
Male, n (%)	180 (54.9)
D-S, n (%)	
IA + 2A + 2B	59 (18.0)
3A	212 (64.6)
3B	57 (17.4)
ISS, n (%)	
1	101 (30.8)
2	102 (31.1)
3	125 (38.1)
R-ISS, n(%)	n = 292
1	33 (11.3)
2	175 (59.9)
3	84 (228.8)
Hgb(g/L), median, (range)	94 (42–161)
Plt, median, (range)	170 (23–597)
WBC, median, (range)	5.1 (1.5–36.6)
MCV (fL), median, (range)	95.2 (72.1-112.3)
Hematopoietic score, n (%)	
0	93 (28.4)
1	103 (31.4)
2	90 (27.4)
3	42 (12.8)
LDH (u/L), median, (range)	188 (79-5785)

Abbreviations: DS, Durie-Salmon Staging; ISS, International Staging System; R-ISS, Revised International Staging System; Hgb, hemoglobin; Plt, platelet; WBC, white blood cell; MCV, mean corpuscular volume; LDH, lactate dehydrogenase; Cr, creatinine; PD, bortezomib, dexamethasone; PCD, bortezomib, dexamethasone, cyclophosphamide; PAD, bortezomib, dexamethasone, adriamycin; PTD, bortezomib, dexamethasone thalidomide; ASCT: Autologous hematopoietic stem cell transplantation.

Baseline characteristics	N = 328
Cr (umol/L), median, (range)	86 (33-1033)
Bone marrow plasma cells %, median, (range)	27 (10–99)
Therapy received, n (%)	
PAD	38 (11.6)
PCD	214 (65.2)
PTD	23 (7.0)
PD	53 (16.2)
ASCT, n (%)	43 (13.1)

Abbreviations: DS, Durie-Salmon Staging; ISS, International Staging System; R-ISS, Revised International Staging System; Hgb, hemoglobin; Plt, platelet; WBC, white blood cell; MCV, mean corpuscular volume; LDH, lactate dehydrogenase; Cr, creatinine; PD, bortezomib, dexamethasone; PCD, bortezomib, dexamethasone, cyclophosphamide; PAD, bortezomib, dexamethasone, adriamycin; PTD, bortezomib, dexamethasone thalidomide; ASCT: Autologous hematopoietic stem cell transplantation.

A MCV > 99.1fL was common in patients with a Hgb level < 100 g/L (34% vs 13%) and bone marrow plasma cells percentage > 30% (31% vs 21%), age ≥ 70 years (37% vs 23%), Plt < 150×10^9/L (36% vs 19%) and high-risk RISS (35% vs 21% vs 21%). A Hgb level < 100 g/L was most common in patients aged ≥ 70 years (74% vs 57%) and was also common in patients with Plt counts < 150×10^9/L (81% vs 47%), bone marrow plasma cells percentage > 30% (69% vs 52%), renal insufficiency (sCr > 177umol/L) (79% vs 56%), high-risk Durie-Salmon stage (81% vs 61% vs 36%), ISS stage (79% vs 65% vs 32%), R-ISS (83% vs 55% vs 18%) stage and elevated red blood cell volumes(80% vs 53%). A Plt count < 150×10^9/L was common in patients with Hb < 100g/L (52% vs 19%), MCV > 99.1fL (55% vs 34%), bone marrow plasma cells percentage > 30% (50% vs 30%), serum LDH > normal level (62% vs 33%), high-risk Durie-Salmon stage (49% vs 41% vs 22%), ISS stage (51% vs 33% vs 30%) and RISS stage (57% vs 33 % vs 24%) **(Supplementary Table 1).**

Hematopoietic Score And Patient Survival

The median duration of follow-up was 32.2 months, the median PFS time was 33.3 months (95%CI: 23.6–43.0), and the estimated 3-year and 5-year PFS rates were 48.0% and 31.0%, respectively. The median OS was 60.5 months (95%CI: 54.1–66.9), and the estimated 3-year and 5-year OS rates were 70.4% and 50.3%, respectively. The patient's age, bone marrow plasma cell percentage, serum LDH level, Durie-Salmon stage and RISS stage significantly affected patient PFS ($P < 0.05$) **(**Table 2, **Supplementary Table 2)**. Moreover the patient's age, Durie-Salmon stage, ISS stage, RISS stage, bone marrow plasma cell

percentage, and serum creatinine and LDH levels had significant effects on OS ($P < 0.05$) (Table 3, **Supplementary Table 2**).

Table 2
Univariable and multivariable analysis for PFS

Univariable analysis			**Multivariable analysis**		
Variable	HR (95%CI)	P value	Variable	HR (95%CI)	P value
Age ≥ 70 years	1.55 (1.10–2.18)	0.013	Age ≥ 70 years	1.43 (0.99–2.06)	0.057
D-S 3B vs 1-3A	1.50 (1.03–2.17)	0.032	Hematopoietic score 2–3 vs 0–1	1.64 (1.19–2.26)	0.003
ISS 3 vs 1–2	1.26 (0.93–1.70)	0.138	Plasma cells > 30%	1.54 (1.12–2.12)	0.008
R-ISS 3 vs 1–2	1.57 (1.12–2.20)	0.009			
WBC < 4×10^9/L	0.93 (0.64–1.34)	0.694			
Hgb < 100g/L	1.24 (0.91–1.67)	0.173			
MCV > 99.1fL	1.58 (1.14–2.18)	0.005			
Plt < 150×10^9/L	1.59 (1.18–2.14)	0.002			
Hematopoietic score 2–3 vs 0–1	1.75 (1.30–2.35)	< 0.001			
Plasma cells > 30%	1.76 (1.31–2.36)	< 0.001			
Cr > 177umol/L	1.34 (0.93–1.93)	0.119			
LDH > 245u/L	1.88 (1.33–2.66)	< 0.001			

Abbreviations: HR, hazard ratio; CI, confidence interval; D-S, Durie-Salmon Staging; ISS, International Staging System; R-ISS, Revised International Staging System; WBC, white blood cell; Hgb, hemoglobin; MCV, mean corpuscular volume; Plt, platelet; Cr, creatinine; LDH, lactate dehydrogenase.

Table 3
Univariable and multivariable analysis for OS

Univariable analysis			**Multivariable analysis**		
Variable	HR (95%CI)	P value	Variable	HR (95%CI)	P value
Age ≥ 70 years	1.76 (1.18–2.62)	0.005	Age ≥ 70 years	1.67 (1.11–2.48)	0.013
D-S 3B vs 1-3A	2.58 (1.73–3.84)	< 0.001	LDH > 245u/L	1.95 (1.31–2.90)	0.001
ISS 3 vs 1–2	2.00 (1.40–2.85)	< 0.001	Hematopoietic score 2–3 vs 0–1	1.60 (1.11–2.31)	0.011
R-ISS 3 vs 1–2	2.51 (1.70–3.71)	< 0.001	Plasma cells > 30%	1.81 (1.26–2.60)	0.001
WBC < 4×10^9/L	0.84 (0.54–1.32)	0.451	Cr > 177umol/L	2.15 (1.44–3.21)	< 0.001
Hgb < 100g/L	1.58 (1.08–2.31)	0.018			
MCV > 99.1fl	1.83 (1.25–2.67)	0.001			
Plt < 150×10^9/L	1.78 (1.25–2.53)	0.001			
Hematopoietic score 2–3 vs 0–1	2.03 (1.43–2.89)	< 0.001			
Plasma cell > 30%	1.97 (1.38–2.81)	< 0.001			
Cr > 177umol/L	2.42 (1.63–3.59)	< 0.001			
LDH > 245u/L	2.25 (1.53–3.30)	< 0.001			

Abbreviations: PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; D-S, Durie-Salmon Staging; ISS, International Staging System; R-ISS, Revised International Staging System; WBC, white blood cell; Hgb, hemoglobin; MCV, mean corpuscular volume; Plt, platelet; Cr, creatinine; LDH, lactate dehydrogenase.

Based on univariable analysis, MCV and platelet counts significantly affect the patient's PFS, while Hgb, MCV and platelet counts significantly affect the patient's OS (Tables 2, 3, **and Supplementary Table 2)**.

The median PFS was 38.7 months for patients with Hgb levels ≥ 100 g/L and 26.5 months for Hgb levels < 100 g/L (*P = 0.173*), and the median OS was 64.8 and 56.8 months, respectively (*P = 0.018*). The median PFS was 38.1 months for patients with MCV ≤ 99.1fL and 23.3 months for patients with MCV > 99.1fL (*P = 0.005*), and the median OS times were 63.1 and 46.2 months, respectively (*P = 0.001)*. Additionally, the median PFS was 42.8 months for patients with Plt counts ≥ 150×10^9/L and 24.1 months for patients with Plt counts < 150×10^9/L (*P = 0.002*), and the median OS times were not reach (NR) vs 51.1 months(*P = 0.001*), respectively. Each of the above three indicators was assigned a score of 1 to generate the hematopoietic score. The integral values were 0, 1, 2, and 3, and the score significantly affected both PFS and OS (P < 0.001) (Tables 2, 3 and Fig. 1A, 1B). Overall, 93 (28.4%), 103 (31.4%),90 (27.4%) and 42 (12.8%) patients had scores of 0, 1, 2 and 3, respectively; the median PFS times were 38.7 months, 55.9 months, 23.9 months and 16.7 months, respectively *(P < 0.001)*, and the median OS times were NR, 64.8 months, 53.6 and 33.2 months, respectively *(P < 0.001)*. The median PFS was 43.1 months in patients who had a hematopoietic score from 0 to 1, and the estimated 3-year and 5-year PFS rates were 54.5% and 37.6%, respectively. In patients with a score of 2–3, the median PFS was only 23.5 months, with estimated 3-year and 5-year PFS rates of 37.3% and 20.6%, respectively (*P < 0.001*) **(**Fig. 2A, Table 1, **Supplementary Table 2)**. The median OS was NR for patients who had a hematopoietic score from 0 to 1, and the estimated 3-year and 5-year OS rates were 78.8% and 56.6%, respectively. In contrast, the median OS of patients who had a score of 2 to 3 was only 31.4 months, with estimated 3-year and 5-year OS rates of 58.0% and 40.7%, respectively (*P < 0.001*) **(**Fig. 2B, Table 2, **Supplementary Table 2).**

Cox proportional hazards model was used for multivariate analysis. The factors that enter the PFS analysis include age, R-ISS stage, bone marrow plasma cell ratio, and hematopoietic score; factors that enter OS analysis include age, ISS stage, serum creatinine and LDH levels, bone marrow plasma cell percentage and hematopoietic score. The results suggested that hematopoietic score (2–3 vs 0–1, HR, 1.64; P = 0.003) and plasma cell percentage (> 30%, HR, 1.54; P = 0.008) were independent prognostic predictors of PFS; The patient's age (> 70 years, HR, 1.67; P = 0.013), serum LDH (> 245u/L, HR, 1.95; P = 0.001), serum creatinine level (> 177umol/L, HR, 2.15; P < 0.001), hematopoietic score (2–3 vs 0–1, HR, 1.60; P = 0.011) and bone marrow plasma cells percentage (> 30%, HR, 1.81; P = 0.001) were independent prognostic predictors of OS (Tables 2, 3).

Discussion

MM is an extremely heterogeneous disease, and survival can range from months to long-term stable disease. Therefore, it is very important to evaluate the prognosis of patients at the time of initial diagnosis. Study has confirmed that the occurrence and development of MM depends on the tumor microenvironment in the bone marrow, and the interaction between myeloma cells and the bone marrow microenvironment is very complicated. In addition to occupying the niches where hematopoietic cells can grow, the proliferation of MM cells can also result in the secretion of a large amount of hematopoietic inhibitory factors, which affect normal hematopoiesis (16, 17), regarding megakaryocytic and erythroid precursor cells in particular, both the number and function are significantly inhibited, including clone

formation ability and self-renewal ability (17). Therefore, low Hgb levels and Plt counts and an increased red blood cell volume may indicate the presence of more plasma cells in the bone marrow. Moreover, normal hematopoietic function is inhibited by various mechanisms, which indicates that the disease is more invasive.

In an early Mayo clinic study (with patients enrolled from 1985 to 1988), it was found that a Hgb level < 100 g/L and a Plt count < 150×10^9/L were predictive of relatively worse outcomes based on univariate analysis (2). In 2020, clinical data of MM patients treated at the Mayo Clinic in the United States for more than 10 years were retrospectively analysed (11), and propose the influence of hematopoietic score composed of Hgb level, MCV and plt count on the prognosis of MM patients, which confirmed that patients with high hematopoietic scores tend to have a worse prognosis. However, those data were obtained for patients in the previous era of traditional chemotherapy, less than 45% of the patients in this group were treated with a proteasome inhibitor and/or immunomodulator-based regimen; therefore, the prognostic significance of the hematopoietic score needs further confirmation in the era of new drugs.

In this study, we evaluated the prognostic effect of hematopoietic score in MM patients treated with a bortezomib-based regimen, and confirmed that hematopoietic score is an independent prognostic predictor for PFS and OS. Our data suggest that Hgb < 100g/L indicates worse OS, which is an important prognostic indicator for newly diagnosed MM patients; an increased MCV similarly suggests worse PFS and OS and these occur more often in patients with Hgb level < 100 g/L and bone marrow plasma cell percentage > 30%. An increased red blood cell volume is often an indication of folic acid or vitamin B12 deficiency; however, it is regrettable that only a few patients in our group were tested for serum vitamin levels, with no deficiency found. According to the literature, vitamin B12 deficiency has been reported in approximately 13–20% of patients with plasma cell disease (11, 18, 19). Regardless, this may not be related to macrocytosis in these patients, and some patients with vitamin B12 deficiency do not show an increase in their MCV (11, 18). It is believed that increased an erythrocyte volume is more common in elderly patients, which may be related to the shortened erythrocyte life span and the emergence of more new erythrocytes (reticulocytes) to replace the lost red blood cells, resulting in a slightly larger volume (20) and an increased peripheral blood red blood cell distribution width (9, 21).

Our study showed that the peripheral blood Hgb level, MCV, and Plt counts all affected PFS and/or OS in MM patients, while the WBC count did not. We also found that among patients older than 70 years old, with high-risk ISS and R-ISS stages, high bone marrow cell percentages and high serum LDH levels were more likely to occur when the Hgb levels were less than 100 g/L, the MCV was above the normal level and/or the Plt count was less than 150×10^9/L. The Hgb level, MCV, and Plt count are each assigned a score of 1 when they deviate from the given parameters, generating the hematopoietic score, which adequately predicts the survival of patients undergoing first-line treatment with a bortezomib-based regimen.

The hematopoietic score is simple and easy to obtain. Indeed, all three indicators can be obtained very readily from routine blood examinations. Furthermore, the score has significant prognostic value in

patients receiving new drug treatments, indicating that it can be used as an important supplement to the R-ISS stage, especially when FISH cannot be routinely performed. However, this study was retrospective, and the number of cases was not large. Furthermore, blood vitamin B12 and folic acid levels were not detected. We intend to further expand the number of cases and re-evaluate the value of the hematopoietic score for prognostic prediction in MM patients in a more standardized prospective study and to combine cytogenetic abnormalities with the ISS stage; by doing so, we aim to establish a new prognostic system for MM patients that is applicable in the era of new drug therapy.

Abbreviations

MM, Multiple myeloma; Hgb, hemoglobin; MCV, mean corpuscular volume; Plt, platelet; PFS, progression-free survival; OS, overall survival; NR, not reached; HR, hazard ratio; ORR, overall response rate; VGPR, very good partial remission; D-S, Durie-Salmon Staging; ISS, International Staging System; R-ISS, Revised International Staging System; LDH, lactate dehydrogenase; FISH, fluorescence in situ hybridization; RDW, red blood cell distribution width; WHO, World Health Organization; IMWG International Myeloma Working Group; PD, progressive disease; WBC, white blood cell; Cr, creatinine; PD, bortezomib and dexamethasone; PCD, bortezomib, dexamethasone and cyclophosphamide; PAD, bortezomib, dexamethasone and adriamycin; PTD, bortezomib, dexamethasone and thalidomide; PR, partial remission; ASCT, hematopoietic stem cell transplantation; CR, complete remission; SD, stable disease; CI, confidence interval.

Declarations

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None.

Author contributions

Jingsong He wrote part of manuscript, reviewed literature, manage the patient and collected clinical data; Xiaoyan Yue translated the manuscript, reviewed and wrote part of the manuscript; XiaoYan Han, DongHua He, Yi Zhao and GaoFeng Zheng reviewed and wrote part of the manuscript, suggested constructively; Yang Yang and WenJun Wu managed the patient, reviewed and wrote part of the manuscript; Zhen Cai wrote part of manuscript, review of literature and suggested constructively. All authors reviewed the manuscript and contributed to the final draft.

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Conflict of interest statement

The authors declare no competing financial interests.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University. All methods were carried out in accordance with relevant guidelines and regulations. Since this is a retrospective study, all patients have signed informed consent during their hospitalization, indicating that all medical data of their examinations and treatments in this hospital may be used as data for publication, but the published article will not disclose the patients and their family's private information, so once the patient signs the informed consent for treatment in our hospital, the informed consent was obtained from all patients.

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Figures

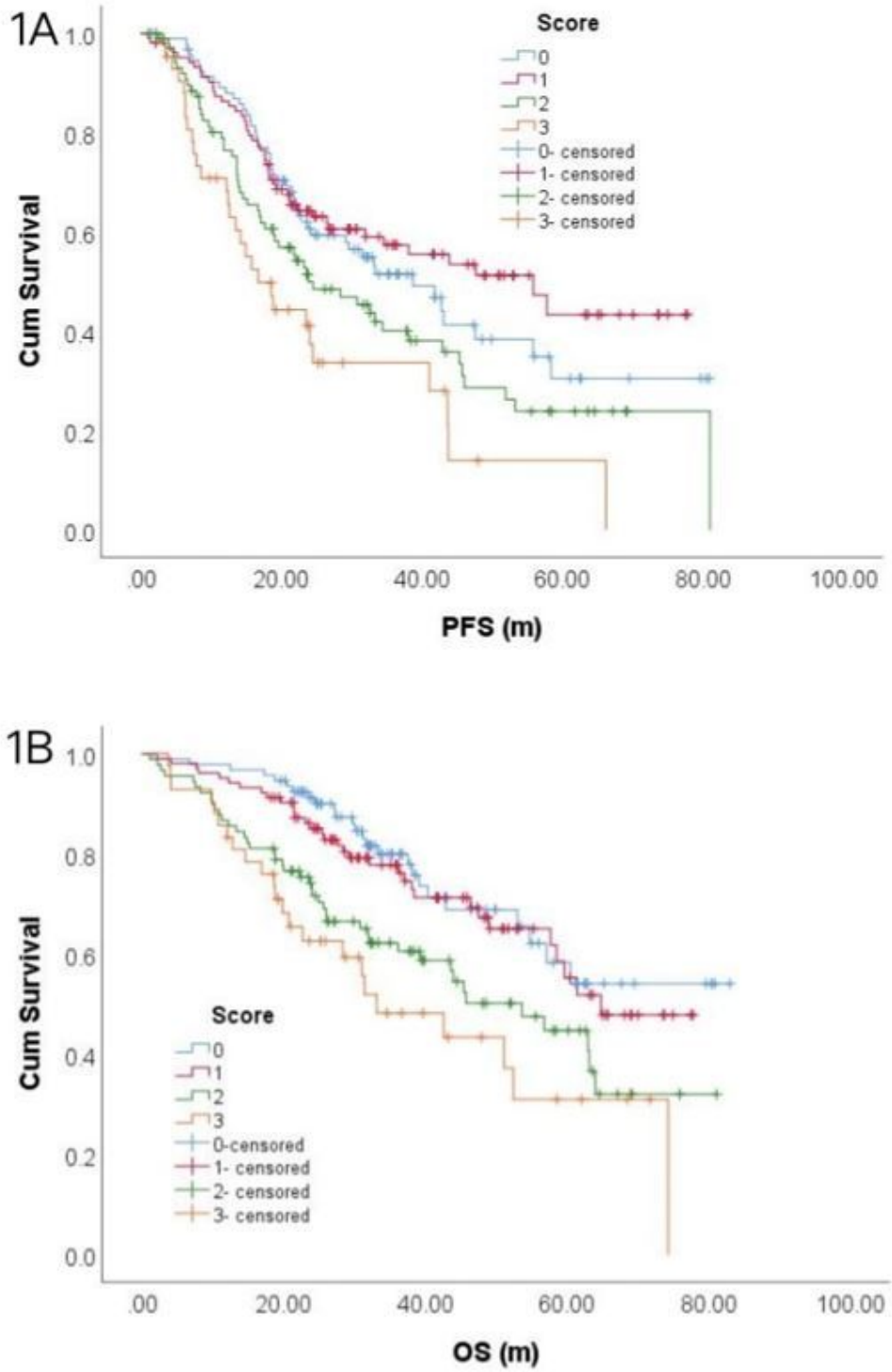

Figure 1

Progression-free survival (1A) and overall survival (1B) based on the hematopoietic score (0, 1, 2, 3

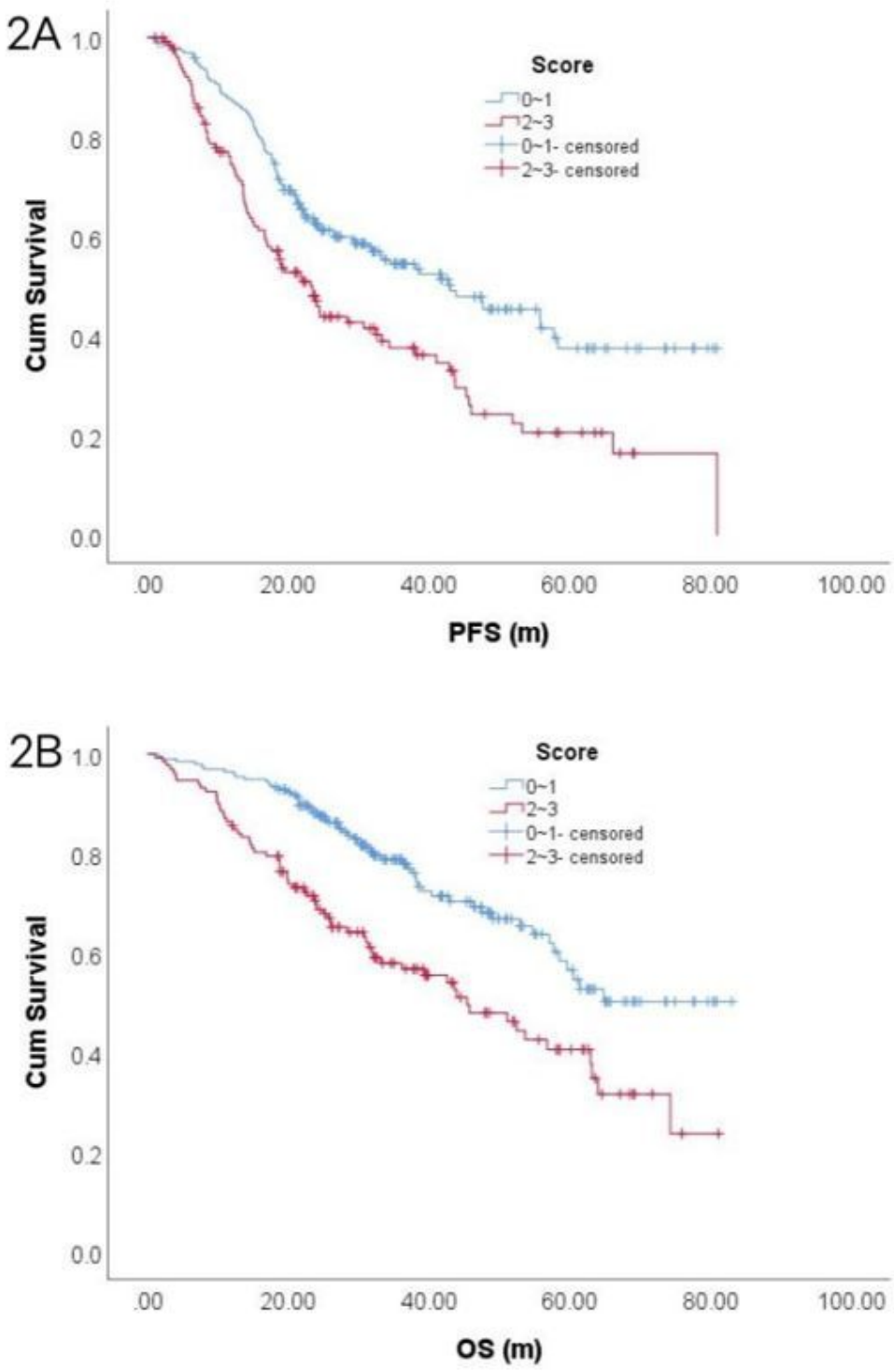

Figure 2

Progression-free survival (2A) and overall survival (2B) based on the hematopoietic score (0-2, 3).

Supplementary Files

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- SupplementaryTable1.docx
- SupplementaryTable2.docx