Impact of perioperative hemoglobin-related parameters on clinical outcomes in patients with spinal metastases: identifying key markers for blood management

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Abstract

Purpose Patients with spinal metastases undergoing surgical treatment face challenges related to preoperative anemia, intraoperative blood loss, and frailty, emphasizing the significance of perioperative blood management. This retrospective analysis aimed to assess the correlation between hemoglobin-related parameters and outcomes, identifying key markers to aid in blood management.

Methods A retrospective review was performed to identify patients who underwent surgical treatment for spinal metastases. Hb-related parameters, including baseline Hb, postoperative nadir Hb, predischarge Hb, postoperative nadir Hb drift, and predischarge Hb drift (both in absolute values and percentages) were subjected to univariate and multivariate analyses. These analyses were conducted in conjunction with other established variables to identify independent markers predicting patient outcomes. The outcomes of interest were postoperative short-term (6-week) mortality, long-term (1-year) mortality, and postoperative 30-day morbidity.

Results A total of 289 patients were included. Our study demonstrated that predischarge Hb (OR 0.62, 95% CI 0.44–0.88, $P = 0.007$) was an independent prognostic factor of short-term mortality, while baseline Hb (OR 0.76, 95% CI 0.66–0.88, $P < 0.001$) was identified as an independent prognostic factor of long-term mortality. Additionally, nadir Hb drift (OR 0.82, 95% CI 0.70–0.97, $P = 0.023$) was found to be an independent prognostic factor for postoperative 30-day morbidity.

Conclusions This study demonstrated that predischarge Hb, baseline Hb, and nadir Hb drift are prognostic factors for outcomes. These findings provide a foundation for precise blood management strategies. It is crucial to consider Hb-related parameters appropriately, and prospective intervention studies addressing these markers should be conducted in the future.

Keywords Spinal metastases, Surgery, Hemoglobin, Blood management, Outcome.

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Background

In addition to the lungs and liver, the spine is also a frequently observed location of malignant metastasis. Approximately 60–70% of patients diagnosed with systemic cancer develop spinal metastases, with about 10% experiencing symptoms [1, 2]. Surgical intervention for patients with spinal metastases offers pain relief, protection, and improvement of neurological function, as well as the maintenance and restoration of spinal stability [3, 4].

In patients with metastatic disease, the presence of preoperative anemia, significant intraoperative blood loss, and frailty underscores the critical clinical importance of perioperative blood management. In the perioperative period, multiple hemoglobin (Hb) monitoring is often conducted. The results at different time points and their correlations are closely associated with postoperative complications and patient prognosis [5–8]. A comprehensive, impartial analysis of the correlation between Hb-related parameters and patient outcomes is crucial for identifying important parameters. It is necessary to implement specific interventions based on these markers to improve patient prognosis.

The baseline Hb level prior to treatment serves as an indicator of the patient's long-term physical condition. The baseline Hb level is included as a prognostic variable in certain scoring systems for spinal metastasis [5, 6]. Nadir Hb refers to the lowest recorded level of Hb for a patient during medical evaluation or monitoring. Postoperative Hb drift is defined as the difference between the preoperative Hb level and the postoperative nadir Hb level [9]. Studies have found these variables to be strongly associated with postoperative complications and prognosis [10–12]. In a few studies, predischarge Hb has also been examined [13–15].

In this study, we analyzed various Hb-related parameters, including baseline Hb, postoperative nadir Hb, predischarge Hb, postoperative nadir Hb drift, and predischarge Hb drift (both in absolute values and percentages). Our objective was to investigate their impact on postoperative morbidity and short- and long-term mortality. By providing these insights, our aim was to provide valuable information to enhance perioperative blood management strategies for patients with spinal metastases. We hope that these markers will attract the attention of clinicians and offer preliminary clues for further study.

Methods

Study participants

We conducted a retrospective review of the medical records of all patients who underwent spinal metastases surgery at our institution between January 2017 and December 2020. This study was approved by the institutional review board of our hospital (no. 2022-437-002).

Therapeutic approaches were managed by a multidisciplinary team, and the decision to perform surgery was based on the patient's medical fitness, clinical presentation (neurological deficits, spinal instability, and intractable pain), oncological status, and the feasibility of surgical treatment.

Two deep incision drains were inserted postoperatively. Anticoagulation therapy was initiated 48–72 hours after surgery. The decision to administer intraoperative transfusion was based on a combination of factors, including blood loss, hemodynamic status, and intraoperative Hb levels. For postoperative transfusion, a threshold of 8 g/dL is typically used as the trigger. No intraoperative cell saver was used. In addition, patient symptoms and underlying medical conditions were considered during the decision-making process.

Follow-ups were prospectively administered to our hospital staff. Following surgery, scheduled follow-up assessments were performed at 3, 6, and 12 months in the first year, followed by semiannual evaluations for the subsequent two years, and annually thereafter.

The inclusion criteria were as follows: (1) a pathologically confirmed diagnosis of spinal metastasis; (2) spinal surgery for excision, osteotomy, decompression, fusion, or fixation; and (3) age greater than 18 years at the time of surgery. The exclusion criteria were as follows: (1) loss to follow-up within one year after surgery, precluding the definitive determination of 1-year survival, (2) underwent unplanned reoperation during hospitalization, and (3) exclusive reliance on percutaneous vertebroplasty.

Hb-related parameters and other factors

Preoperative blood tests were performed as part of standard patient evaluation. Routine blood tests were performed on the first postoperative day and monitored every 2–4 days unless indications of severe anemia or increased drainage were evident. The baseline Hb level was determined based on the most recent Hb level prior to surgery. The nadir Hb level was defined as the lowest postoperative Hb level recorded during hospitalization. The predischarge Hb level was defined as the final Hb test result before patient discharge. Absolute nadir Hb drift was defined as the difference between the baseline and postoperative nadir Hb levels. The percentage nadir Hb drift was calculated as (baseline Hb - nadir Hb) / baseline Hb × 100%. Absolute predischarge Hb drift was determined as the difference between the baseline and predischarge Hb levels. The percentage of predischarge Hb drift was computed as (baseline Hb–predischarge Hb) / baseline Hb × 100%.

The following variables were analyzed in conjunction with Hb-related parameters: age, primary tumor site (classified as slow, moderate, or rapid growth according to the classification proposed by Katagiri [7]), visceral

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metastases, number of spine metastases, presence of other bone metastases, Eastern Cooperative Oncology Group (ECOG) performance status, American Spinal Injury Association (ASIA) Impairment Scale, and transfusion.

Outcome measures
The outcomes of interest were postoperative short-term (6-week) mortality, long-term (1-year) mortality, and postoperative 30-day morbidity. Although 30-day mortality was also used in many studies as short-term mortality, this study opted for a 6-week postoperative criterion due to the lower short-term mortality rates in Asian populations [16, 17] and to mitigate the occurrence of fewer outcome events. The postoperative morbidities included in this study were systemic infection, pneumonia, cardiac arrest/failure/arrhythmia, myocardial infarction, delirium, stroke, venous thromboembolism, gastrointestinal bleeding, urinary tract infection, wound infection, and/or dehiscence [18–20].

Statistical analysis
Continuous variables were summarized as mean and standard deviation, while categorical variables were presented as frequencies and percentages. Initial univariate logistic regression analyzed each factor, and those with $P<0.10$ underwent multivariate logistic regression with backward stepwise elimination. For correlated Hb-related parameters (absolute and percentage drift), only the variable with the lowest P value underwent multivariate analysis. In the final model, $P<0.05$ was considered significant. The optimal cutoff value for plotting the survival curve was determined through logistic regression, selecting the split with the highest significance using the "cutoff " package in R. We performed statistical analysis using R version 4.1.3 for Windows (R Project for Statistical Computing, http://www.r-project.org/).

Results
Patient demographics and clinical outcomes
A total of 289 patients (138 male, 151 female) with an average age of 55.7±10.5 were included in this study, adhering to the inclusion and exclusion criteria. Among the primary tumor site pathologies, lung cancer ($n=79$, 27.3%) was the most prevalent, followed by breast cancer ($n=56$, 19.4%), liver cancer ($n=18$, 6.2%), and kidney cancer ($n=13$, 4.5%). With reference to Katagiri's classification of primary tumor sites of malignancy [7], 103 (36%) patients are of slow growth, 75 (26%) patients are of moderate growth, and 111 (38%) patients are of rapid growth. There were 37 patients with an ECOG score of 37, 62 with a score of 2, 90 with a score of 3, and 100 with a score of 4.

The baseline Hb level was 12.3±1.8 g/dL, the nadir Hb was 9.7±1.8 g/dL, and the predischarge Hb was 10.8±1.6 g/dL. According to the formula presented above, the absolute nadir Hb drift was −2.6±1.7 g/dL, and the percentage nadir Hb drift was −21% ± 13%. The absolute predischarge Hb drift was −1.6±1.9 g/dL, and the percentage predischarge Hb drift was −12% ± 15%. The demographic and clinical characteristics of the patients are presented in Table 1.

The short-term (6-week) mortality, was 5.5%. The long-term (1-year) mortality was 45.3%. Postoperative morbidity within 30 days occurred in 20.4% of patients, including 16 cases of pneumonia,14 cases of systemic infection, 13 cases of wound infection and/or dehiscence, 5 cases of venous thromboembolism, 4 cases of myocardial infarction and delirium, and 3 cases of stroke.

The baseline characteristics and outcomes of patients with different surgery types are summarized in Table S1.

Correlation between Hb-related parameters and clinical outcomes
In the study, univariate analysis identified factors associated with short-term mortality, including nadir Hb, predischarge Hb, primary tumor site, visceral metastases, and ASIA. In the multivariate analysis, predischarge Hb remained independently associated with short-term mortality (OR 0.61, 95% CI 0.42–0.87, $P=0.006$) (Table 2). Figure 1 showed a rapid risk reduction of postoperative short-term mortality with increasing Hb levels, plateauing around 9.5 g/dL. According to the method described above, the optimal cut-off value for predischarge Hb was 9.7 g/dL. The survival curves for patients with predischarge Hb levels greater and less than 9.7 g/dL are shown in Fig. 2.

Long-term mortality associations included baseline Hb, nadir Hb, predischarge Hb, absolute predischarge Hb drift (only the absolute value of predischarge Hb drift was included in the multivariate model due to its lower P value compared to the predischarge Hb drift in percentage), the primary tumor site, number of spine metastases, and ECOG performance. In the multivariate analysis, baseline Hb remained independently associated with long-term mortality rate (OR 0.82, 95% CI 0.68–0.99, $P=0.039$) (Table 3). Figure 3 indicated decreasing long-term mortality with increasing baseline Hb, plateauing near 13.0 g/dL. The optimal cut-off value for the baseline Hb level was 11.5 g/dL. The survival curves for patients with baseline Hb levels above and below 11.5 g/dL are shown in Fig. 4.

For 30-day morbidity, only the nadir Hb drift in absolute value and visceral metastases were subjected to the multivariate analysis. Absolute nadir Hb drift remained independently associated with the 30-day morbidity rate (OR 0.82, 95% CI 0.70–0.97, $P=0.023$) (Table 4). Figure 5

Table 1 Baseline characteristics of the patients (*n* = 289)

Factors	Value
Age (years)	55.7 ± 10.5
Male sex	138 (48%)
Primary tumor site	
Slow growth	103 (36%)
Moderate growth	75 (26%)
Rapid growth	111 (38%)
Location	
Cervical	23 (8.0%)
Thoracic	159 (55%)
Lumbar-Sacral	77 (27%)
Combined	30 (10%)
No. of spine metastases	
1 level	92 (32%)
2 levels	35 (12%)
≥ 3 levels	162 (56%)
ECOG performance status	
Score 0–2	99 (34%)
Score 3–4	190 (66%)
Other bone metastases	187 (65%)
ASIA scale	
A to C	56 (19%)
D or E	233 (81%)
Visceral metastases	127 (44%)
Surgery type	
Corpectomy with stabilization	137 (47%)
Decompression and stabilization	79 (27%)
Decompression alone	73 (25%)
Prior local radiotherapys	29 (10%)
Previous systemic therapys	162 (56%)
Blood loss (ml)	1128.3 ± 1053.5
Transfusions	189 (65%)
Baseline Hb (g/dL)	12.3 ± 1.8
Postoperative nadir Hb (g/dL)	9.7 ± 1.8
Predischarge Hb (g/dL)	10.8 ± 1.6
Nadir Hb drift	
Absolute (g/dL)	−2.6 ± 1.7
Percentage	−21% ± 13%
Predischarge Hb drift	
Absolute (g/dL)	−1.6 ± 1.9
Percentage	−12% ± 15%

ECOG, Eastern Cooperative Oncology Group; ASIA, American Spinal Injury Association

displayed a high morbidity probability for absolute nadir Hb drift values less than −3 g/dL, decreasing rapidly with increasing drift. Beyond −1.5 g/dL, the morbidity probability plateaued or slightly elevated.

Discussion

In this study, we systematically assessed the prognostic significance of Hb-related parameters in patients with spinal metastases undergoing surgery, filling a gap in existing research. Predischarge Hb levels independently predicted short-term mortality, while baseline Hb levels prognosticated long-term mortality. Absolute nadir Hb drift emerged as an independent prognostic factor for 30-day morbidity. Our findings underscore the crucial role of perioperative blood management and highlight specific markers for improved patient outcomes. This study, the first of its kind in the context of spinal metastases, emphasizes the importance of vigilant monitoring and timely interventions in enhancing patient prognosis.

Surgical interventions benefit symptomatic spinal metastases patients, but intraoperative bleeding is a significant challenge due to tumor hypervascularity and

Table 2 Univariate and multivariate analysis of the factors related to postoperative short-term (6-week) mortality

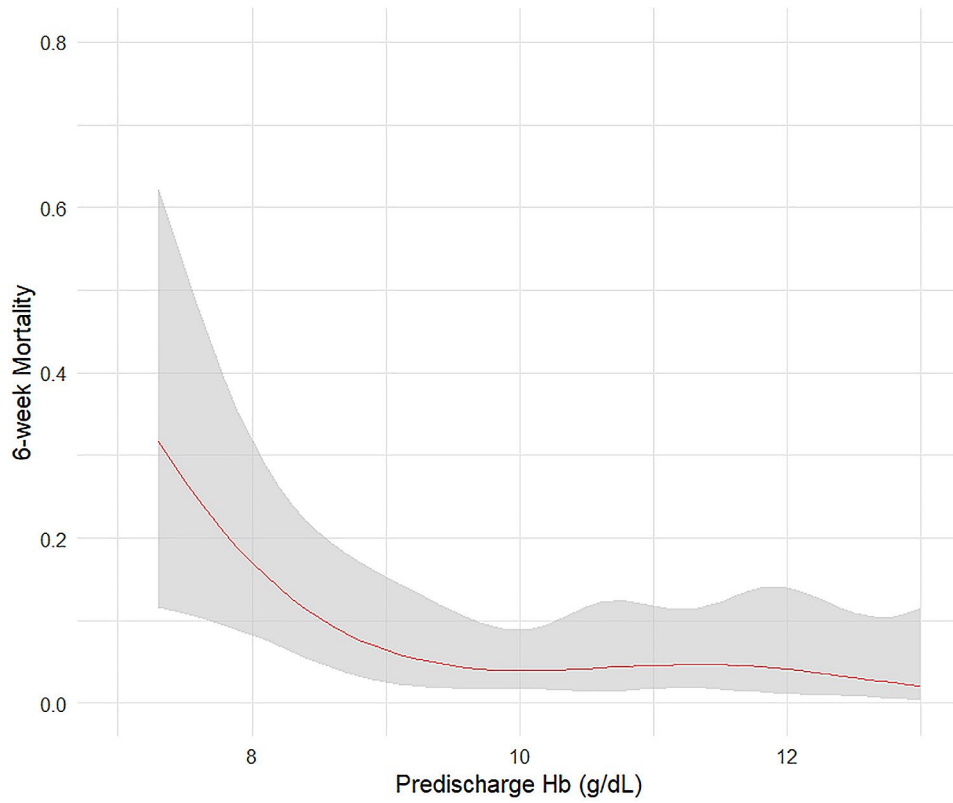| Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Baseline Hb	0.89 (0.67–1.16)	0.384		
Postoperative nadir Hb	0.75 (0.57-1.00)	0.048		
Predischarge Hb	0.62 (0.44–0.88)	0.007	0.61 (0.42–0.87)	0.006
Nadir Hb drift				
Absolute	0.85 (0.64–1.12)	0.239		
Percentage	0.05 (0.00-2.38)	0.127		
Predischarge Hb drift				
Absolute	0.80 (0.61–1.06)	0.116		
Percentage	0.03 (0.00-1.66)	0.087		
Age	0.98 (0.94–1.03)	0.522		
Primary tumor site				
Slow growth	Ref		Ref	
Moderate growth	7.46 (0.85–65.34)	0.070	6.03 (0.65–55.86)	0.114
Rapid growth	9.49 (1.18–76.38)	0.034	8.57 (1.02–72.25)	0.048
Visceral metastases	2.70 (0.90–8.14)	0.077		
No. of spine metastases				
1 level	Ref			
2 levels	2.25 (0.57–8.90)	0.250		
≥ 3 levels	0.79 (0.24–2.55)	0.688		
Other bone metastases	2.47 (0.69–8.86)	0.167		
ECOG				
Score 0–2	Ref			
Score 3–4	2.08 (0.57–7.58)	0.265		
ASIA				
A to C	Ref		Ref	
D or E	0.26 (0.09–0.75)	0.013	0.16 (0.05–0.49)	0.002
Transfusion	1.17 (0.40–3.48)	0.772		
Blood loss > 1000 ml	0.76 (0.26–2.26)	0.624		
Surgery type				
Corpectomy with stabilization	Ref			
Decompression and stabilization	0.99 (0.28–3.49)	0.988		
Decompression alone	1.37 (0.42–4.46)	0.606		
30-day morbidity	2.49 (0.87–7.16)	0.090		

ECOG, Eastern Cooperative Oncology Group; ASIA, American Spinal Injury Association

dilated epidural veins [21], resulting in an average blood loss of 2,180 mL [22]. The unique physical characteristics of oncology patients and bleeding risks highlight the critical need for perioperative blood management. Balancing surgical risks and blood resource consumption is essential. Investigating the clinical relevance of Hb-related parameters and their correlations with treatment outcomes is crucial for a rational approach to blood management in these cases.

Postoperative short-term mortality is common among patients with spinal metastases [23, 24], indicating that surgical decision-making does not primarily offer palliative results. Previous studies have predominately focused on preoperative prognostic factors and baseline variables. However, in this study, the predischarge Hb level was identified as an independent prognostic factor for short-term mortality, which has not been previously studied

in the field of spinal metastases. This can serve as an early warning indicator for identifying high-risk patients prior to discharge. Our findings suggest that maintaining Hb levels > 10.0 g/dL before discharge can significantly improve patient outcomes. For patients with lower predischarge Hb levels, close monitoring is suggested.

In this study, we identified lower baseline Hb level as an independent prognostic factor for postoperative 1-year mortality in patients with spinal metastases. One possible explanation for this finding is that anemia serves as an indicator of the underlying comorbid disease burden and physiological reserve, which are pivotal factors in achieving long-term survival. The evaluation of systemic components in patients with spinal metastases is critical for surgical decision-making, especially considering the increased fragility of these patients due to disease progression, treatments, and cachexia [25]. Anemia is

Fig. 1 The restricted cubic spline figure between predischarge Hb and postoperative short-term (6-week) mortality
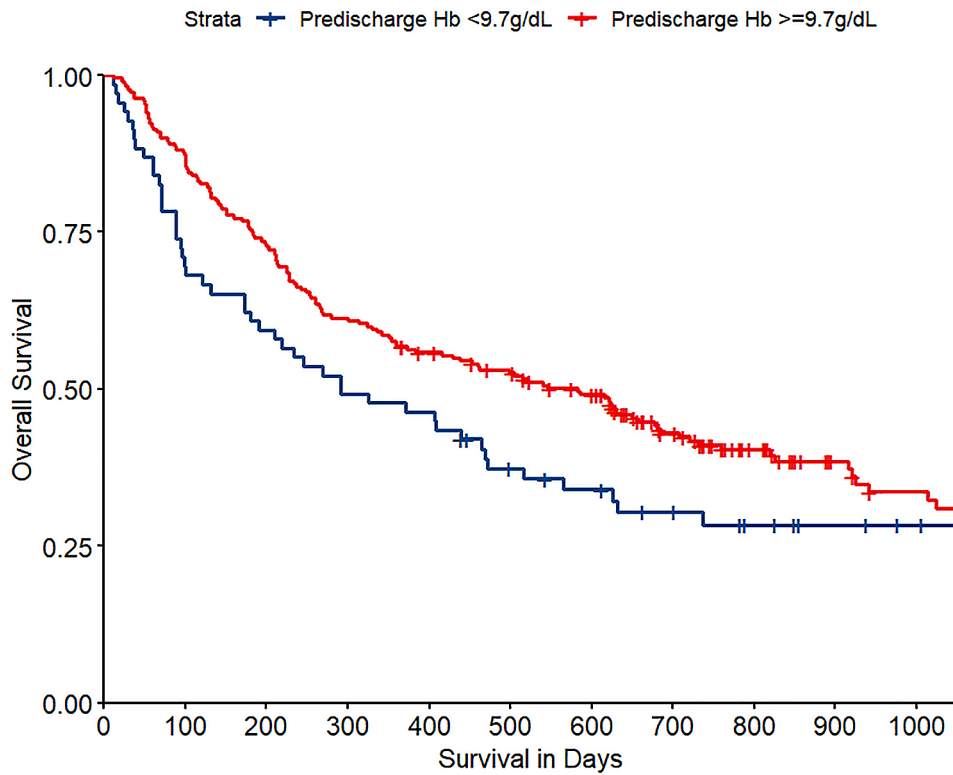
Fig. 2 Kaplan-Meier curve of overall survival for patients with predischarge Hb < 9.7 g/dL and ≥ 9.7 g/dL

Table 3 Univariate and multivariate analysis of the factors related to postoperative long-term (1-year) mortality
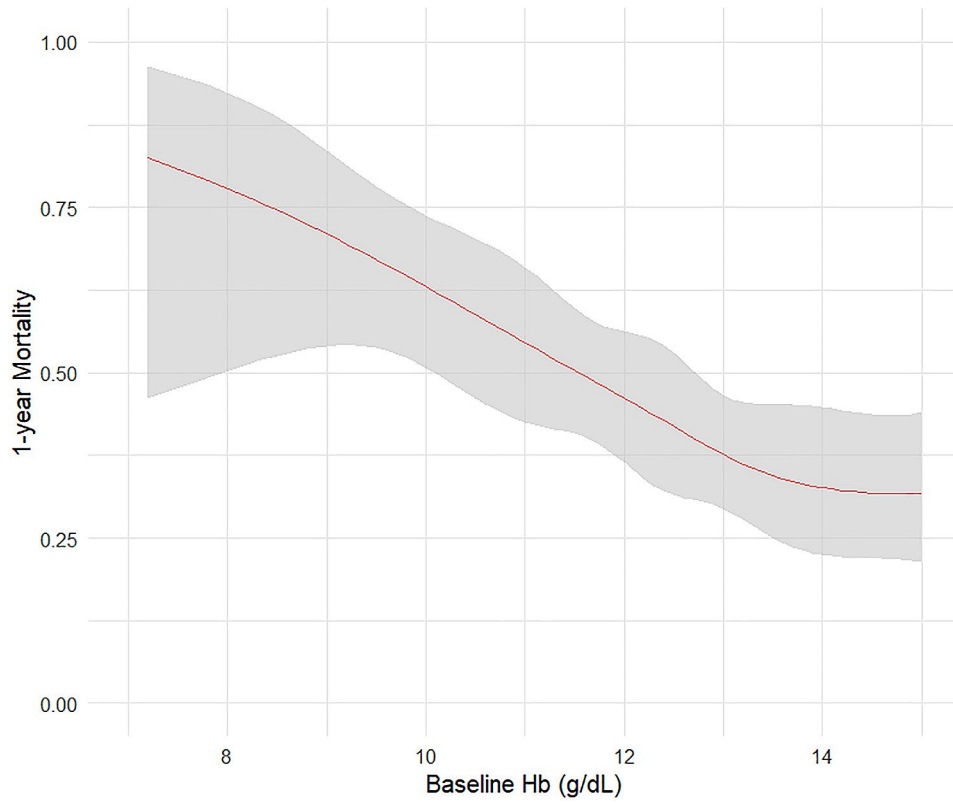
Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Baseline Hb	0.76 (0.66–0.88)	< 0.001	0.82 (0.68–0.99)	0.039
Postoperative nadir Hb	0.84 (0.74–0.96)	0.009		
Predischarge Hb	0.88 (0.77–1.02)	0.091		
Nadir Hb drift				
Absolute	1.10 (0.96–1.27)	0.152		
Percentage	2.04 (0.34–12.05)	0.432		
Predischarge Hb drift				
Absolute	1.17 (1.03–1.33)	0.016		
Percentage	7.14 (1.42–35.83)	0.017		
Age	1.01 (0.99–1.03)	0.354		
Primary tumor site				
Slow growth	Ref		Ref	
Moderate growth	2.59 (1.36–4.91)	0.004	3.3063450 1.6138291 6.9572681	0.001
Rapid growth	5.76 (3.18–10.45)	< 0.001	7.9279341 3.9575718 16.6267541	< 0.001
Visceral metastases	1.44 (0.90–2.30)	0.126		
No. of spine metastases				
1 level	Ref		Ref	
2 levels	2.68 (1.21–5.96)	0.016	2.7888459 1.0993837 7.2847946	0.033
≥ 3 levels	1.62 (0.96–2.74)	0.072	1.5532853 0.7849035 3.1158877	0.209
Other bone metastases	1.30 (0.80–2.11)	0.295		
ECOG				
Score 0–2	Ref		Ref	
Score 3–4	3.22 (1.90–5.46)	< 0.001	2.4252384 1.2857389 4.6674838	0.007
ASIA				
A to C	Ref			
D or E	0.35 (0.19–0.64)	< 0.001		
Transfusion	0.96 (0.59–1.56)	0.868		
Blood loss > 1000 ml	0.60 (0.37–1.27)	0.685		
Surgery type				
Corpectomy with stabilization	Ref			
Decompression and stabilization	0.91 (0.52–1.60)	0.733		
Decompression alone	2.01 (1.13–3.58)	0.018		

ECOG, Eastern Cooperative Oncology Group; ASIA, American Spinal Injury Association

a common manifestation of frailty, particularly prevalent among oncology patients due to direct and indirect causes [26]. The impaired oxygen-carrying capacity caused by the presence of anemia may contribute to multiple clinical manifestations of cancer, including fatigue, dyspnea, dizziness, and exhaustion. Notably, cancer-related anemia significantly affects patients' quality of life and is associated with an elevated risk of mortality and treatment-related adverse events [27]. Prediction scoring systems for survival in metastatic spine disease should consider incorporating baseline Hb as an important predictor [5, 6]. Consequently, we confirm that steady-state Hb levels in patients can serve as a marker for long-term survival. Aggressive interventions focusing on the etiology of anemia and nutritional supplementation have the potential to benefit patients.

Nadir Hb drift was initially researched by Karkouti et al., who found that nadir Hb drift, rather than nadir Hb, was independently associated with an increased risk of adverse outcomes in cardiac surgery [28]. Similar associations have been reported in various surgical contexts, including gastrointestinal surgery [11], head and neck surgery [12], brain tumor surgery [10], and non-oncological spinal surgery [8]. These studies recommended considering postoperative Hb drift in addition to Hb levels when assessing the need for transfusion. Our research indicates that postoperative morbidity is associated with nadir Hb drift rather than nadir Hb alone. As previously mentioned, a patient's baseline Hb level is influenced by the underlying comorbid disease and the physiological reserve state to which the patient has adapted to a certain degree. Consequently, the body may exhibit greater sensitivity to a relative change in Hb level than to a specific low value. Research has shown that patients with abnormally high Hb levels may not tolerate sudden Hb reductions, even if their Hb levels remain within the normal

Fig. 3 The restricted cubic spline figure between baseline Hb and postoperative long-term (1-year) mortality
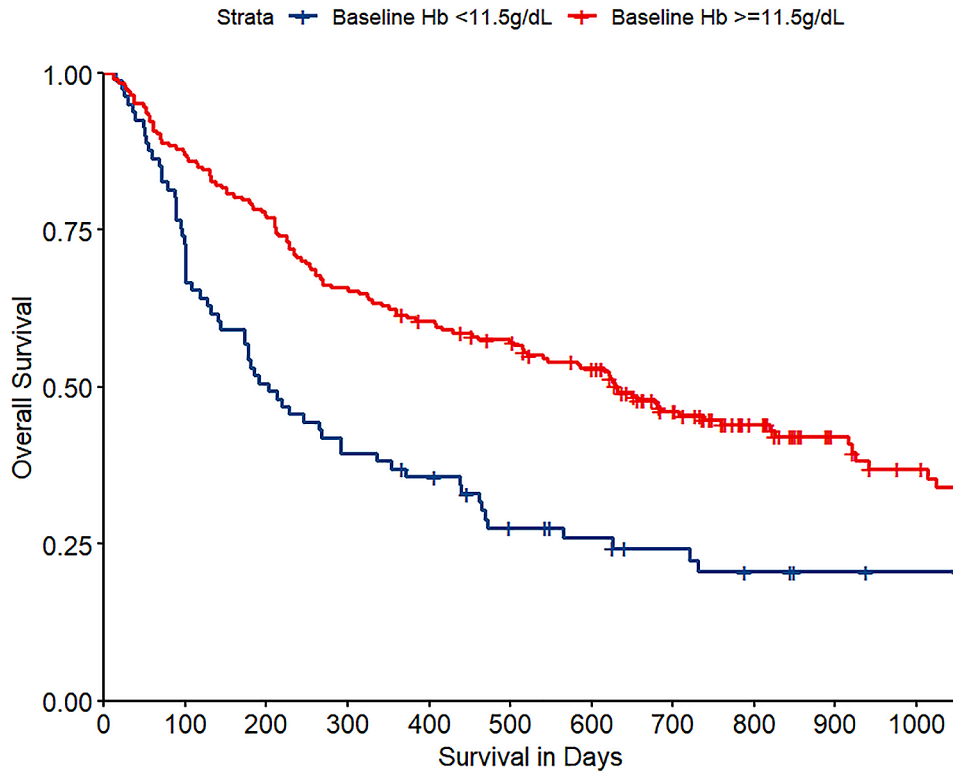
Fig. 4 Kaplan-Meier curve of overall survival for patients with baseline Hb < 11.5 g/dL and ≥ 11.5 g/dL

Table 4 Univariate and multivariate analysis of the factors related to postoperative 30-day morbidity

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Baseline Hb	1.05 (0.90–1.23)	0.528		
Postoperative nadir Hb	0.88 (0.75–1.03)	0.113		
Predischarge Hb	0.95 (0.80–1.13)	0.568		
Nadir Hb drift				
Absolute	0.82 (0.70–0.97)	0.021	0.82 (0.70–0.97)	0.023
Percentage	0.07 (0.01–0.67)	0.022		
Predischarge Hb drift				
Absolute	0.91 (0.78–1.07)	0.259		
Percentage	0.44 (0.06–3.21)	0.418		
Age	1.00 (0.97–1.02)	0.791		
Primary tumor site				
Slow growth	Ref			
Moderate growth	0.85 (0.41–1.73)	0.646		
Rapid growth	0.60 (0.31–1.19)	0.144		
Visceral metastases	1.68 (0.95–2.99)	0.076		
No. of spine metastases				
1 level	Ref			
2 levels	0.60 (0.21–1.75)	0.349		
≥ 3 levels	0.96 (0.51–1.78)	0.888		
Other bone metastases	0.98 (0.54–1.79)	0.957		
ECOG				
Score 0–2	Ref			
Score 3–4	1.69 (0.89–3.22)	0.112		
ASIA				
A to C	Ref			
D or E				
Transfusion	1.39 (0.75–2.60)	0.296		
Blood loss > 1000 ml	1.11 (0.62-2.00)	0.727		
Surgery type				
Corpectomy with stabilization	Ref			
Decompression and stabilization	1.05 (0.52–2.14)	0.893		
Decompression alone	1.58 (0.80–3.11)	0.189		

ECOG, Eastern Cooperative Oncology Group; ASIA, American Spinal Injury Association

range, because they require above-normal Hb levels to ensure adequate oxygen delivery to tissues [29]. To minimize Hb fluctuations, bleeding control techniques such as minimally invasive surgery and preoperative embolization should be considered. Additionally, maintaining hemodynamic stability through rational blood transfusion is crucial. Notably, minor reductions did not increase the probability of persistent complications. This is demonstrated in Fig. 5, where the risk of complications reaches a plateau or may even slightly increase above −1.5 g/dL, possibly owing to the adverse effects of allogeneic blood transfusion. Therefore, there is no need for excessive transfusions, and consideration should be given to the scarcity of blood resources and the adverse effects of transfusions.

This study has several limitations that should be acknowledged when interpreting the findings. Firstly, it was an observational study, and the efficacy of a focused

intervention on these significant parameters in improving patient outcomes remains to be established. Secondly, owing to disparities in healthcare policies, patients across various countries receive varying levels of medical support after discharge. However, the effects of predischarge Hb levels may differ. Thirdly, further studies are required to investigate the importance of Hb-related parameters in various patient subgroups.

Conclusions

Our study illustrates that various perioperative Hb-related parameters correlate with the prognosis of patients with spinal metastases. Predischarge Hb, baseline Hb, and nadir Hb drift were independent prognostic factors for postoperative short- and long-term mortality and surgical morbidity, respectively. These correlations remained statistically significant even after conducting multifactorial analyses, considering other established

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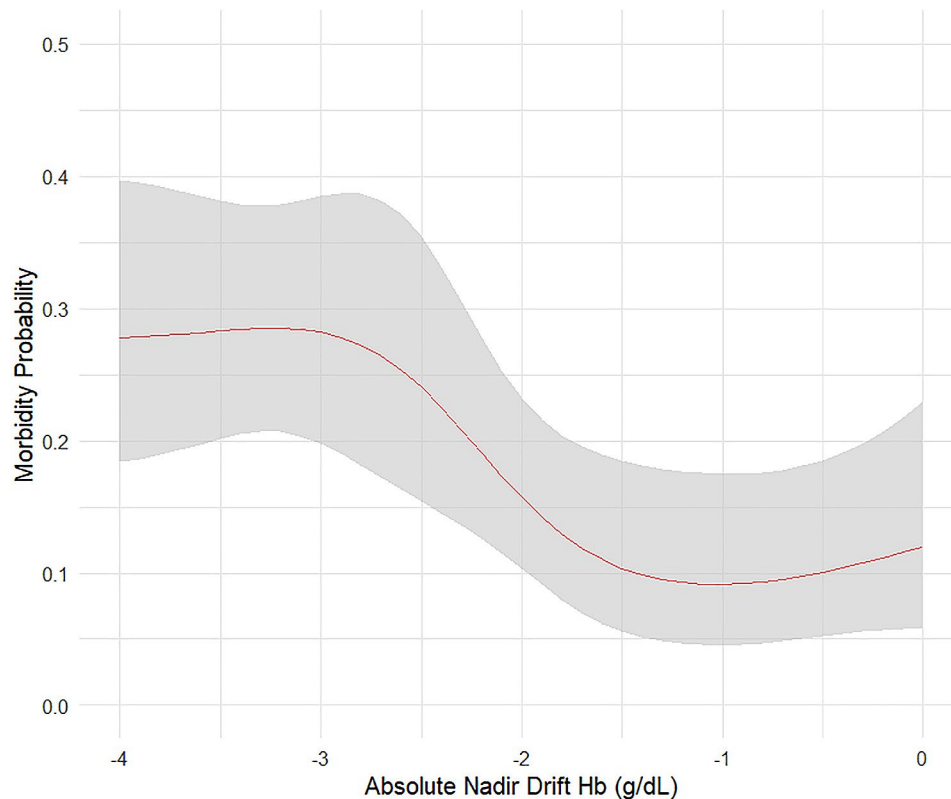
Fig. 5 The restricted cubic spline figure between nadir Hb drift and postoperative 30-day morbidity

variables. Our findings provide a foundation for precise blood management. It is crucial to appropriately assess Hb-related parameters, and prospective intervention studies addressing these markers should be conducted in the future.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12891-024-07748-9.

Supplementary Material 1

Declarations

Ethical approval and consent to participate
This study was approved by the institutional review board of Affiliated Cancer Hospital of Zhengzhou University (no. 2022-437-002). Clinical information were obtained from medical management systems of hospital. All methods were carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients and/or their legal guardian(s).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
None.

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