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Smoking is a significant contributor to intraoperative blood loss in metastatic spinal tumor surgery: a propensity score analysis

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Abstract

Background Metastatic spinal tumors pose a significant challenge regarding intraoperative blood loss. Identifying risk factors for intraoperative blood loss is crucial for appropriate surgical planning and early intervention. However, current studies have not comprehensively evaluated risk factors for predicting intraoperative blood loss. This study aims to determine whether smoking significantly contributes to intraoperative blood loss among metastatic spinal tumors and to investigate other potential risk factors.

Methods This study analyzed 252 patients with metastatic spinal disease who underwent posterior decompressive surgery, and the primary outcome measured was intraoperative blood loss, with massive intraoperative blood loss defined as exceeding 2500 mL. Propensity score matching analysis was employed to analyze the influence of smoking on intraoperative blood loss. In addition, subgroup analysis was performed based on smoking status before and after propensity score analysis. Multivariate analysis was used to analyze the relationship between smoking and intraoperative blood loss. To assess the predictive value of smoking status for intraoperative massive blood loss, we conducted an analysis using the Area Under the Receiver Operating Characteristic Curve (AUROC), and the corresponding Area Under the Curve (AUC) values were subsequently calculated.

Results Before conducting the propensity score analysis, the study found that smoking patients had a significantly higher volume of intraoperative blood loss (1938.30 mL vs. 1722.32 mL, $P=0.014$) and a greater incidence of massive intraoperative blood loss (36.4% vs. 20.1%, $P=0.008$) compared to non-smokers. After adjusting for propensity scores, the results showed that smokers still had a higher volume of intraoperative blood loss (1938.30 mL vs. 1703.41 mL, $P=0.019$) and a higher proportion of massive intraoperative blood loss (39.7% vs. 14.9%, $P=0.002$) than non-smokers. Multiple linear regression analysis confirmed that smoking status was significantly associated with intraoperative

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blood loss before (Estimate = 1.410, $P = 0.001$) and after (Estimate = 1.443, $P = 0.010$) propensity score matching analysis. Additionally, the logistic regression demonstrated that smokers were 2.268 times (95% CI: 1.272–4.044) more likely to experience intraoperative massive blood loss compared to nonsmokers before propensity score analysis ($P = 0.005$). After propensity score analysis, the fold increase in risk further rose to 3.764 (95% CI: 1.643–8.621), indicating an even stronger association between smoking and intraoperative blood loss ($P = 0.002$). Furthermore, the AUC value increased from 0.596 (95% CI: 0.527–0.666) for smoking status before propensity score matching analysis to 0.660 (95% CI: 0.567–0.753) after propensity score matching analysis.

Conclusions Smoking is a significant risk factor for increased intraoperative blood loss and should be taken into consideration when planning surgical interventions for patients with metastatic spinal tumors.

Keywords Smoking, Intraoperative blood loss, Metastatic spinal tumors, Propensity score matching analysis, Risk factors

Introduction

Metastatic spinal tumors are a common consequence of advanced-stage malignancy, and their incidence is increasing due to improvements in cancer treatments and prolonged survival [1]. Approximately 40% of cancer patients will experience vertebral metastases, and 20% of these cases will result in neurological deterioration due to spinal instability, spinal cord compression, or cauda equina compression [2, 3]. These metastatic tumors can cause significant morbidity and mortality, and their management often requires complex surgical interventions [4]. Studies have shown that surgical decompression of the neural elements in metastatic spinal tumors leads to better outcomes compared to radiotherapy alone, particularly in terms of ambulatory function, continence, and alleviation of pain [5, 6].

However, intraoperative blood loss is a major concern during surgical procedures. It is estimated that the average intraoperative blood loss for metastatic spinal tumors ranges from 1490 mL [7] to 2180 mL [8], with some cases experiencing catastrophic blood loss of over 5500 mL [8]. Excessive blood loss can lead to hemodynamic instability, prolonged hospital stays, and increased morbidity [9]. Furthermore, the use of blood transfusions during surgery for metastatic spinal disease may increase the risk of early postoperative complications, such as sepsis [10], deep vein thrombosis [10], prolonged ventilation [10], and surgical site infection [11]. Therefore, there is great interest in the field for decreasing intraoperative blood loss in metastatic spinal tumor surgery.

Notably, smoking is a well-established risk factor for various malignancies, including lung, breast, head and neck, bladder, and pancreatic cancers [12]. Additionally, it has been found to be associated with an increased risk of postoperative complications in surgical procedures for metastatic spinal tumors, such as wound infections [13, 14], delayed healing, and pulmonary complications, prolonged length of hospital stay [15], non-routine discharge [15], in-hospital mortality [15], and decreased survival outcome [16]. Several studies have also indicated a significant association between smoking and intraoperative blood loss in patients undergoing spine surgery. Specifically, this relationship has been demonstrated in lumbar spine surgery for lumbar disc protrusion [17], complex deformity surgery [18], and various other surgical procedures [19]. In addition, our previous study notably identified smoking as a key predictor to establish prediction models for assessing intraoperative massive blood among patients with metastatic spinal disease treated with decompressive surgery [20]. While this study highlighted smoking as an important factor affecting intraoperative blood loss, it was based on subgroup analysis, leaving the causal relationship unexamined. Understanding this relationship is crucial, as it may have significant implications for surgical planning and patient management. If smoking is confirmed to be a causal factor, it could lead to the development of targeted interventions aimed at reducing intraoperative blood loss and improving surgical outcomes.

Therefore, to addresses this gap in knowledge, this study conducted a propensity score analysis to investigate the causal association between smoking and intraoperative blood loss in patients undergoing surgical management of metastatic spinal tumors. We hypothesize that smoking significantly contributes to increased intraoperative blood loss among patients undergoing posterior decompressive surgery for metastatic spinal disease. We anticipate that the analysis will reveal a strong association between smoking and heightened intraoperative blood loss, underlining the importance of considering smoking status as a critical factor in surgical planning for patients with metastatic spinal tumors.

Patients and methods

Inclusive and exclusive criteria

This study analyzed 252 patients with metastatic spinal disease treated with posterior decompressive surgery between January 2011 and December 2022 from two large medical institutes. Patients were considered eligible for inclusion if they exhibited MRI evidence of

metastatic spinal disease alongside one or more of the following symptoms: (1) worsening local mechanical or radiation-induced pain; (2) progressive sensory impairments; (3) motor function deficits in the lower limbs; or (4) impairments in sphincter function. Surgical indications included intractable pain and myelopathy due to spinal cord compression resulting from spinal instability. The decision to proceed with surgery was made collaboratively by experienced neuro-radiologists, spinal tumor surgeons, and oncologists. Patients were excluded from analysis if they met any of the following criteria: (1) primary spine tumor; (2) metastatic spinal disease resulting from leukemia; (3) intramedullary metastasis of spinal metastasis; or (4) abstain from smoking for more than three months. The study was approved by the research ethics board of the Peking University First Hospital, and written informed consent was obtained from all patients. Additionally, this study was conducted in accordance with the Declaration of Helsinki, and the work has been reported in line with the STROCSS criteria [21].

Surgical technique

Under general anesthesia, the patient was positioned prone on the operating table. A midline incision was made over the affected spinal region, followed by careful dissection of the muscles to expose the posterior spine. The procedure was carried out via a posterior approach, with laminectomy or laminotomy performed to gain access to the spinal cord and nerve roots. A combination of partial vertebrectomy and tumor debulking was used to remove the tumor. The extent of vertebrectomy was determined by the degree of tumor involvement, with the decision to proceed with subtotal or total vertebrectomy based on the surgeon's assessment of the tumor's characteristics and the patient's overall health. After tumor resection, pedicle screw instrumentation was employed to stabilize the spine. This involved placing screws into the vertebral pedicles, which were then connected with rods to ensure stability and prevent deformity. Chief surgeons performing these procedures were highly experienced spine surgeons with advanced qualifications and over ten years of surgical experience, which ensured a consistent application of surgical techniques among the surgeons involved.

Primary outcomes

The primary outcome was intraoperative blood loss, and the following equation was used to calculate the total blood loss on a surgical day: The total blood loss = theoretical total blood loss + allogeneic blood transfusion, and the theoretical total blood loss = estimated blood volume × 2 × (preoperative hematocrit − postoperative hematocrit)/ (preoperative hematocrit + postoperative hematocrit) [22–24]. In this study, massive intraoperative blood loss was defined as the intraoperative blood loss of 2500 mL or above [25]. The secondary outcome was the length of hospital stay, defined as the time from admission to discharge. Additionally, the length of stay following surgery was assessed, which was the period between the surgery date and discharge.

Collection of clinical characteristics

This study collected patient's demographics (age, gender, BMI [Body Mass Index], and KPS [Karnofsky Performance Scale]), smoking status, comorbidities (diabetes and hypertension), tumor information (primary tumor type, extra-vertebral bone metastasis, and visceral metastasis), preoperative chemotherapy, preoperative embolization, surgical details (surgical process, surgical site, number of surgical segments), and preoperative laboratory examinations (hypoalbuminemia, thrombocytopenia, PT [Prothrombin Time], APTT [Activated Partial Thromboplastin Time]).

Hypoalbuminemia was defined as the protein albumin in the blood less than 35 g/L, and thrombocytopenia was defined as the platelets in the blood less than 100×10^9/L. Smoking status was classified into no vs. yes, and it was also categorized into none vs. short term vs. long term smokers according to the duration of smoking. Patients with the smoking history of more than 30 years were regarded as long-term smokers, whereas patients with the smoking history of 30 years and below were considered as short-term smokers. In this study, data accuracy was ensured through team training, double-entry verification, and rigorous validation checks.

Propensity score matching analysis

Propensity score matching analysis was utilized to account for confounding variables and minimize potential baseline disparities between smokers and non-smokers. Propensity scores were computed using a psmatch model that incorporated all variables that differed between the two groups prior to the propensity score matching analysis [26]. A "match method = nearest" algorithm with a 1:2 ratio and a "caliper width = 0.150" was employed to establish two new cohorts that had more comparable baseline characteristics based on the propensity scores. Standardized mean differences (SMD) were evaluated in the study. In this study, a "match method = nearest" algorithm was utilized for propensity score matching analysis, and this algorithm was chosen because it is widely used and has been shown to be effective in reducing selection bias in observational studies [27]. The matching ratio used was 1:2, which means that for each treated individual, two control individual was selected for comparison, if applicable. This ratio was selected to ensure a sufficient number of control individuals for accurate comparison and to improve the precision of the estimated treatment effect

[28]. To further enhance the accuracy of the matching process, a "caliper width = 0.150" was applied. The caliper width is a parameter that determines the maximum allowable difference in propensity scores between matched pairs. A smaller caliper width ensures that the matched pairs are more closely similar in terms of their propensity scores, thereby reducing potential bias in the estimation of treatment effects [29, 30]. SMD was calculated for each baseline clinical characteristic before and after propensity score analysis. SMD is a measure used to quantify the difference in means between two groups, considering the standard deviation of each group. It is often used in propensity score analysis to assess the balance between groups in terms of baseline characteristics after applying propensity score matching or weighting.

Statistical analysis

In this study, qualitative data were presented as proportions, while quantitative data that did not follow a normal distribution were expressed as interquartile ranges (IQR). Subgroup analyses of baseline clinical characteristics based on smoking status were conducted using the Chi-square test or the Mann-Whitney U test, depending on the data type. Additionally, subgroup analyses of outcomes were performed based on smoking status (no vs. yes) and smoking duration (none vs. short-term vs. long-term) using the Chi-square test, the Mann-Whitney U test or Wilcoxon test. Multiple linear regression analysis was utilized to examine the association between clinical variables, including smoking status, and the amount of intraoperative blood loss. Logistic regression was employed to analyze the relationship between smoking and intraoperative massive blood loss. To evaluate the predictive performance of smoking status and smoking duration for intraoperative massive blood loss, Area Under the Receiver Operating Characteristic Curve (AUROC) analysis was conducted, and the area under the curve (AUC) value was calculated. All statistical analyses were performed using R programming software (R version 4.1.2), and a P-value of less than 0.05 was considered statistically significant.

Results

Patient's baseline clinical characteristic

A total of 252 patients were collected for analysis in this study. Among those patients, 65.5% patients were male, and the median age of all patients was 60.0 [53.00, 67.00] years (Table 1). The most common primary tumor was rapid growth tumors (37.3%), followed by moderate growth tumors (35.3%). The median BMI was 24.14 [21.25, 26.44] kg/m^2. The most common comorbidity was hypertension, accounting for 33.7% of patients. Of all patients, only 18.3% received chemotherapy. The tumor burden was relatively considerable, with 52.1% of patients having a KPS of 50 or lower, and 24.2% exhibiting visceral metastases. The vast majority of patients were treated with palliative decompressive surgery (90.1%), with 67.5% of surgical site being thoracic and thoracolumbar and 56.0% of surgical segments being two or above. Patients with hypoalbuminemia and thrombocytopenia were 13.1% and 2.8%, respectively. In addition, the median volume of blood loss was 1820.44 [1284.71, 2565.35] mL in the entire cohort, with 25.8% of patients diagnosing with intraoperative massive blood loss.

Patient's baseline clinical characteristics stratified by smoking status before and after propensity score matching analysis

Before propensity score matching, smoking patients were more likely to have moderate or rapid-growing tumors ($P = 0.005$), be younger ($P = 0.010$), and male ($P < 0.001$). They also had a higher incidence of hypertension ($P = 0.029$) and prolonged APTT ($P = 0.047$) compared to non-smokers (Table 1). These findings indicate a lack of comparability in the clinical characteristics between the two groups.

After propensity score analysis, all baseline clinical characteristics were similarly distributed, with all P values of more than 0.180, indicating comparable clinical characteristics (Table 2). Figure 1 demonstrated that the matched set was much more similar to the matched control set than the raw treated and the control set. In addition, the distribution of propensity scores was much more similar between the matched treated and the control units than between the unmatched units. The SMD before and after propensity score analysis, revealing a significant decrease in the majority of SMDs after propensity score analysis, particularly for primary tumor, hypertension, gender, age, and APTT, all of which were significant different between groups before propensity score matching analysis. For example, the SMD of gender decreased from 1.203 before propensity score matching analysis to 0.006, and the SMD for APTT decreased from 0.281 to 0.074, indicating a perfectly comparable distribution of these variables after matching.

Subgroup analysis of outcomes based on smoking status before and after propensity score matching analysis

Before propensity score matching analysis, smoking patients experienced significantly higher levels of intraoperative blood loss (1938.30 mL vs. 1722.32 mL, $P = 0.014$, Fig. 2A), a greater proportion of massive intraoperative blood loss (36.4% vs. 20.1%, $P = 0.008$), and longer length of hospital stays (20.50 days vs. 18.00 days, $P = 0.027$) compared to non-smokers (Table 3). Additionally, intraoperative blood loss was significantly associated with the length of hospital stays (R square = 0.24, and

Table 1 Patient's baseline clinical characteristics and subgroup analysis of clinical characteristics among patients with and without smoking before propensity score analysis

Characteristics	Overall	Smoking		*P* value	SMD
		No	Yes		
n	252	164	88		
Primary tumor type (%)				0.005	0.448
Slow	69 (27.4)	55 (33.5)	14 (15.9)		
Moderate	89 (35.3)	49 (29.9)	40 (45.5)		
Rapid	94 (37.3)	60 (36.6)	34 (38.6)		
Age (years, median [IQR])	60.00 [53.00, 67.00]	61.00 [53.00, 70.00]	58.00 [52.75, 61.00]	0.010	0.395
Gender (male/female, %)	165/87 (65.5/34.5)	81/83 (49.4/50.6)	84/4 (95.5/4.5)	< 0.001	1.203
BMI (kg/m^2, years, median [IQR])	24.14 [21.25, 26.44]	24.01 [22.06, 25.99]	24.37 [20.68, 27.02]	0.627	0.196
Diabetes (no/yes, %)	214/38 (84.9/15.1)	140/24 (85.4/14.6)	74/14 (84.1/15.9)	0.932	0.035
Hypertension (no/yes, %)	167/85 (66.3/33.7)	117/47 (71.3/28.7)	50/38 (56.8/43.2)	0.029	0.306
Preoperative chemotherapy (no/yes, %)	206/46 (81.7/18.3)	136/28 (82.9/17.1)	70/18 (79.5/20.5)	0.623	0.087
Extra-vertebral bone metastasis (no/yes, %)	134/118 (53.2/46.8)	92/72 (56.1/43.9)	42/46 (47.7/52.3)	0.256	0.168
Visceral metastases (no/yes, %)	191/61 (75.8/24.2)	125/39 (76.2/23.8)	66/22 (75.0/25.0)	0.951	0.028
KPS (> 50/≤50, %)	123/129 (48.8/51.2)	77/87 (47.0/53.0)	46/42 (52.3/47.7)	0.501	0.107
Preoperative embolization (no/yes, %)	233/19 (92.5/7.5)	153/11 (93.3/6.7)	80/8 (90.9/9.1)	0.665	0.088
Surgical process (%)				0.342	0.185
Palliative decompression	227 (90.1)	149 (90.9)	78 (88.6)		
Partial resection of vertebrae	14 (5.6)	10 (6.1)	4 (4.5)		
En bloc resection of vertebrae	11 (4.4)	5 (3.0)	6 (6.8)		
Surgical site (%)				0.603	0.130
Cervical and cervical thoracic	13 (5.2)	7 (4.3)	6 (6.8)		
Thoracic and thoracolumbar	170 (67.5)	110 (67.1)	60 (68.2)		
Lumbar and lumbosacral	69 (27.4)	47 (28.7)	22 (25.0)		
Number of surgical segments (1/≧2, %)	111/141 (44.0/56.0)	75/89 (45.7/54.3)	36/52 (40.9/59.1)	0.547	0.097
Hypoalbuminemia (no/yes, %)	219/33 (86.9/13.1)	145/19 (88.4/11.6)	74/14 (84.1/15.9)	0.439	0.126
Thrombocytopenia (no/yes, %)	245/7 (97.2/2.8)	159/5 (97.0/3.0)	86/2 (97.7/2.3)	1.000	0.048
PT (< 12/≥12, %)	198/54 (78.6/21.4)	128/36 (78.0/22.0)	70/18 (79.5/20.5)	0.908	0.037
APTT (< 32/≥32, %)	143/109 (56.7/43.3)	101/63 (61.6/38.4)	42/46 (47.7/52.3)	0.047	0.281

IQR, Interquartile range; BMI, Body mass index; KPS, Karnofsky performance status; PT, Prothrombin time; APTT, Activated partial thromboplastin time

$P < 0.001$), indicating a higher intraoperative blood loss might lead to a longer length of hospital stays.

After conducting the propensity score analysis, smokers still exhibited a significantly higher median volume of intraoperative blood loss (1938.30 mL vs. 1703.41 mL, $P = 0.019$, Fig. 2B) and a greater proportion of intraoperative massive blood loss (39.7% vs. 14.9%, $P = 0.002$). However, the length of hospital stays lost its significance, with the median of 19 days in both groups ($P = 0.898$), indicating that smoking did not increase the length of hospital stays. Additionally, intraoperative blood loss was not significantly associated with length of hospital stays after propensity score matching analysis (R square = 0.07, and $P = 0.460$).

Subgroup analysis of outcomes based on smoking exposure duration before and after propensity score analysis

Before propensity score analysis, the data indicates notable differences in blood loss and the incidence of intraoperative massive blood loss across the smoking exposure duration subgroups (Table 4). Both short-term and long-term smokers exhibited higher median intraoperative blood loss ($P = 0.003$, Fig. 3A) and a higher proportion of massive blood loss ($P = 0.001$) compared to non-smokers. However, there were no substantial differences in the length of hospital stay ($P = 0.076$). After the propensity score analysis, similar patterns were observed, with significant variations in intraoperative blood loss ($P = 0.007$, Fig. 3B) and the occurrence of massive blood loss ($P = 0.001$) among the three smoking exposure duration groups. Once again, no substantial differences were found in the length of hospital stay ($P = 0.940$) and the length of hospital stay after surgery ($P = 0.069$) across the three subgroups. Overall, the findings suggest a potential correlation between smoking exposure duration and adverse postoperative outcomes, particularly in relation to intraoperative blood loss and the incidence of massive blood loss during surgery.

Table 2 Patient's baseline clinical characteristics and subgroup analysis of clinical characteristics among patients with and without smoking after propensity score analysis

Characteristics	Overall	Smoking		*P* value	SMD
		No	Yes		
n	132	74	58		
Primary tumor (%)				0.219	0.309
Slow	35 (26.5)	23 (31.1)	12 (20.7)		
Moderate	47 (35.6)	22 (29.7)	25 (43.1)		
Rapid	50 (37.9)	29 (39.2)	21 (36.2)		
Age (years, median [IQR])	61.00 [54.00, 68.00]	63.00 [53.25, 69.00]	60.00 [57.00, 63.00]	0.182	0.217
Gender (male/female, %)	123/9 (93.2/6.8)	69/5 (93.2/6.8)	54/4 (93.1/6.9)	1.000	0.006
BMI (kg/m^2, years, median [IQR])	23.59 [21.22, 26.23]	23.72 [22.17, 26.26]	23.51 [20.76, 26.23]	0.301	0.001
Diabetes (no/yes, %)	118/14 (89.4/10.6)	67/7 (90.5/9.5)	51/7 (87.9/12.1)	0.843	0.084
Hypertension (no/yes, %)	90/42 (68.2/31.8)	51/23 (68.9/31.1)	39/19 (67.2/32.8)	0.986	0.036
Preoperative chemotherapy (no/yes, %)	111/21 (84.1/15.9)	63/11 (85.1/14.9)	48/10 (82.8/17.2)	0.896	0.065
Extra-vertebral bone metastasis (no/yes, %)	62/70 (47.0/53.0)	38/36 (51.4/48.6)	24/34 (41.4/58.6)	0.335	0.201
Viscera metastases (no/yes, %)	102/30 (77.3/22.7)	57/17 (77.0/23.0)	45/13 (77.6/22.4)	1.000	0.013
KPS (> 50/≤50, %)	64/68 (48.5/51.5)	38/36 (51.4/48.6)	26/32 (44.8/55.2)	0.569	0.131
Preoperative embolization (no/yes, %)	121/11 (91.7/8.3)	67/7 (90.5/9.5)	54/4 (93.1/6.9)	0.832	0.094
Surgical process (%)				0.436	0.231
Palliative decompression	120 (90.9)	67 (90.5)	53 (91.4)		
Partial resection of vertebrae	5 (3.8)	4 (5.4)	1 (1.7)		
En bloc resection of vertebrae	7 (5.3)	3 (4.1)	4 (6.9)		
Surgical site (%)				0.688	0.151
Cervical and cervical thoracic	7 (5.3)	3 (4.1)	4 (6.9)		
Thoracic and thoracolumbar	97 (73.5)	54 (73.0)	43 (74.1)		
Lumbar and lumbosacral	28 (21.2)	17 (23.0)	11 (19.0)		
Number of surgical segments (1/≧2, %)	53/79 (40.2/59.8)	33/41 (44.6/55.4)	20/38 (34.5/65.5)	0.319	0.208
Hypoalbuminemia (no/yes, %)	110/22 (83.3/16.7)	63/11 (85.1/14.9)	47/11 (81.0/19.0)	0.695	0.110
Thrombocytopenia (no/yes, %)	129/3 (97.7/2.3)	71/3 (95.9/4.1)	58/0 (100.0/0.0)	0.336	0.291
PT (< 12/≥12, %)	108/24 (81.8/18.2)	61/13 (82.4/17.6)	47/11 (81.0/19.0)	1.000	0.036
APTT (< 32/≥32, %)	71/61 (53.8/46.2)	41/33 (55.4/44.6)	30/28 (51.7/48.3)	0.806	0.074

IQR, Interquartile range; BMI, Body mass index; KPS, Karnofsky performance status; PT, Prothrombin time; APTT, Activated partial thromboplastin time

Risk factors for intraoperative blood loss before and after propensity score analysis

Prior to conducting propensity score analysis, multiple linear regression analysis revealed several significant risk factors for intraoperative blood loss, including smoking ($P = 0.001$), primary tumor ($P = 0.007$), preoperative chemotherapy ($P = 0.041$), surgical process ($P = 0.034$), number of surgical segments ($P = 0.027$), and APTT ($P = 0.008$) (Table 5). Upon conducting propensity score analysis, we confirmed that smoking ($P = 0.010$), surgical process ($P = 0.009$), number of surgical segments ($P = 0.017$), and APTT ($P = 0.045$) remained significant risk factors for intraoperative blood loss. The above results indicates that smoking, extensive surgical procedures, and prolonged APTT were associated with greater intraoperative blood loss.

The results of the logistic regression analysis showed that smokers were 2.268 times (95% CI: 1.272–4.044) more likely to experience intraoperative massive blood loss compared to nonsmokers before propensity score analysis ($P = 0.005$) (Fig. 4), indicating that smoking was associated with an increased risk of significant blood loss during surgery. Furthermore, long-term smokers had an even higher odds ratio (OR) of 3.970 (95% CI: 1.863–8.460), indicating that they faced an even greater likelihood of intraoperative massive blood loss compared to nonsmokers ($P < 0.001$). After conducting propensity score matching analysis, the OR for smokers compared to nonsmokers increased to 3.764 (95% CI: 1.643–8.621, $P = 0.002$). Additionally, the OR for long-term smokers versus short-term and non-smokers rose to 6.168 (95% CI: 2.292–16.599, $P < 0.001$). These findings indicate a stronger association between smoking and intraoperative massive blood loss.

In addition, AUROC was used to evaluate the predictive performance of smoking status and smoking duration (in years) for intraoperative massive blood loss. The results showed that before propensity score matching analysis, the AUC value was 0.596 (95% CI: 0.527–0.666) for smoking status (Fig. 5A) and 0.615 (95% CI: 0.541–0.689) for smoking duration (Fig. 5B). After propensity score matching analysis, the AUC values increased to

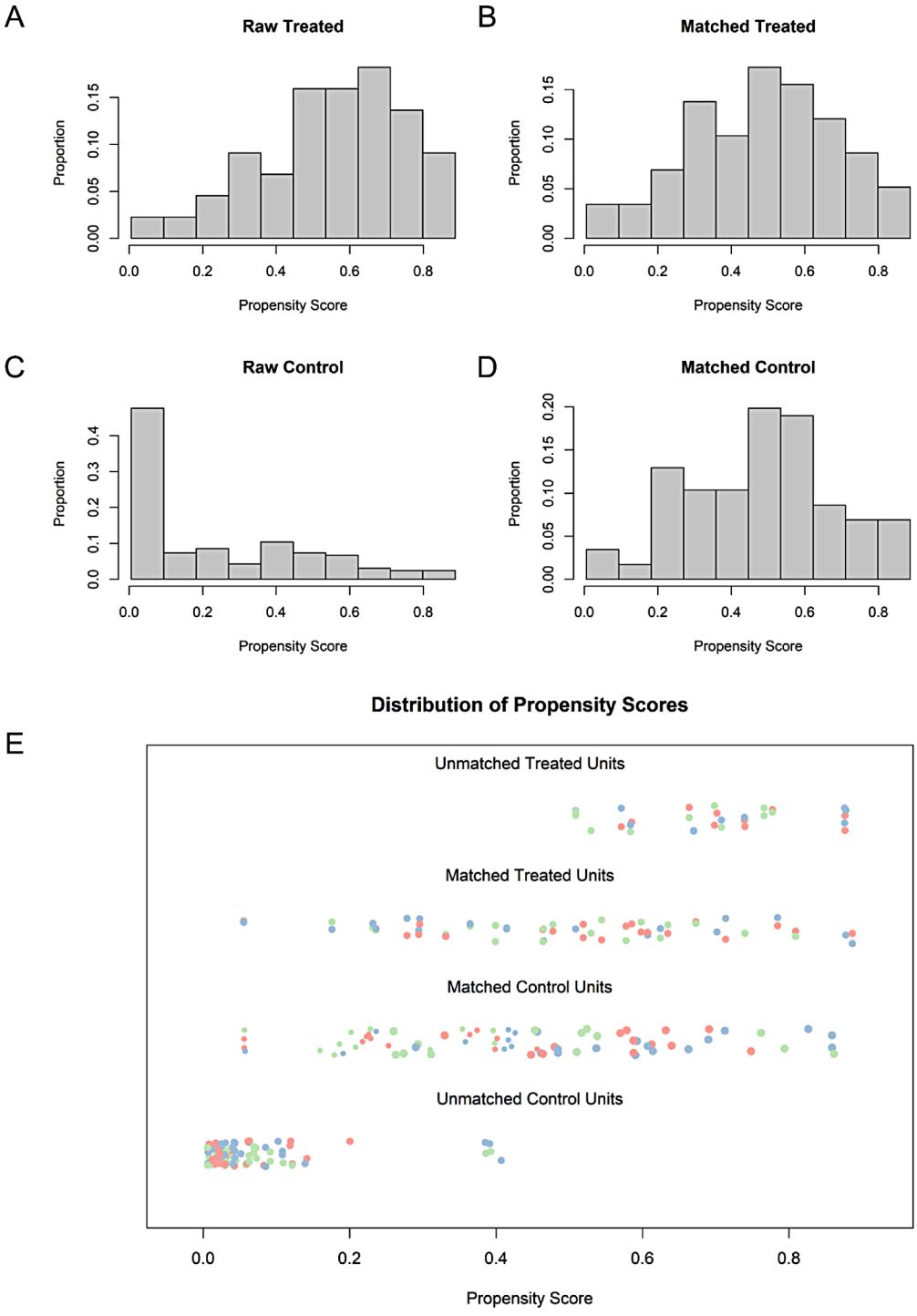

Fig. 1 Distribution of propensity scores before and after propensity score analysis. (**A**) The proportion of propensity score in the raw treated group (smoking patients); (**B**) The proportion of propensity score in the matched treated group; (**C**) The proportion of propensity score in the raw control group (non-smoking patients); (**D**) The proportion of propensity score in the matched control group; (**E**) Scatter plot for distribution of propensity scores before and after propensity score analysis

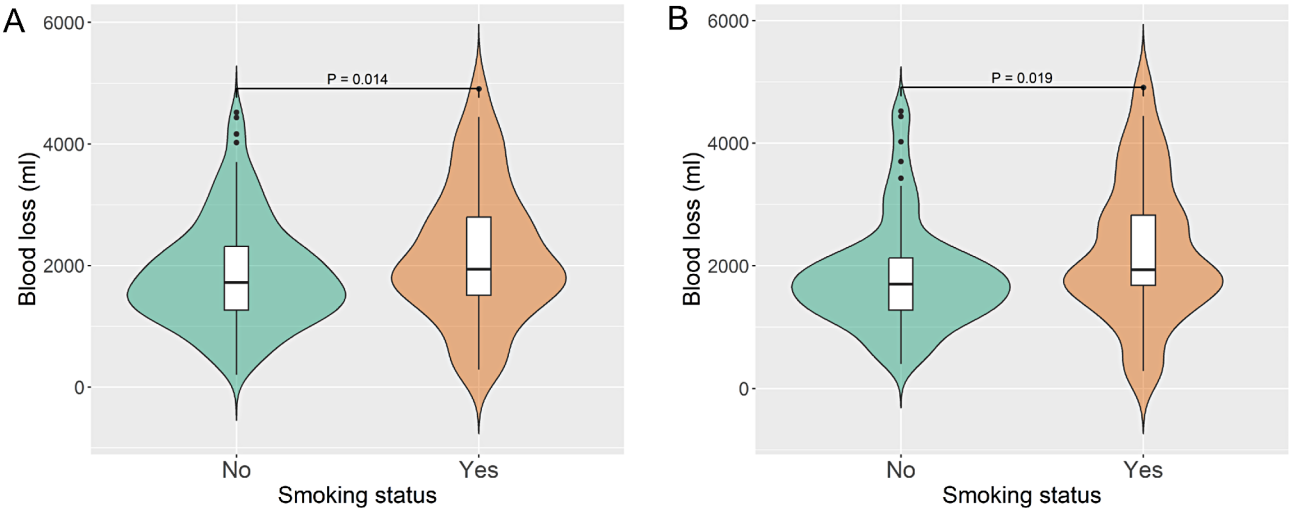

Fig. 2 Violin plot for the distribution of intraoperative blood loss based on the presence of smoking. (**A**) Before propensity score matching analysis; (**B**) After propensity score matching analysis

Table 3 Subgroup analysis of outcomes according to the presence of smoking status before and after propensity score matching analysis

Outcomes	Overall	Smoking status		*P* value
		No	Yes	
Before propensity score matching analysis				
n	252	164	88	
Blood loss (mL, median [IQR])	1820.44 [1284.71, 2565.35]	1722.32 [1265.94, 2312.19]	1938.30 [1511.84, 2795.67]	0.014
Intraoperative massive blood loss (no/yes, %)	187/65 (74.2/25.8)	131/33 (79.9/20.1)	56/32 (63.6/36.4)	0.008
Length of hospital stay (days, median [IQR])	18.00 [14.00, 25.00]	18.00 [14.00, 24.00]	20.50 [15.75, 26.75]	0.027
Length of hospital stay after surgery (days, median [IQR])	14.00 [11.00, 17.25]	13.00 [11.00, 16.00]	14.00 [11.00, 20.00]	0.082
After propensity score matching analysis				
n	132	74	58	
Blood loss (mL, median [IQR])	1815.00 [1310.19, 2572.20]	1703.41 [1277.81, 2124.82]	1938.30 [1680.41, 2826.36]	0.019
Intraoperative massive blood loss (no/yes, %)	98/34 (74.2/25.8)	63/11 (85.1/14.9)	35/23 (60.3/39.7)	0.002
Length of hospital stay (days, median [IQR])	19.00 [14.00, 26.00]	19.00 [14.00, 26.00]	19.00 [14.00, 24.00]	0.898
Length of hospital stay after surgery (days, median [IQR])	13.00 [9.75, 16.00]	13.00 [10.00, 16.00]	14.00 [9.00, 17.50]	0.881

IQR, Interquartile range

0.660 (95% CI: 0.567–0.753) for smoking status (Fig. 5C) and 0.690 (95% CI: 0.589–0.792) for smoking duration (Fig. 5D), indicating more favorable ability to predict intraoperative massive blood loss based on smoking history.

Discussion

Key findings

Our study aimed to investigate the association between smoking and intraoperative blood loss in patients undergoing surgical management of metastatic spinal tumors. We found that smoking was a significant contributor to intraoperative blood loss, as smoking patients had significantly higher intraoperative blood loss and a higher rate of massive intraoperative blood loss than non-smokers. After controlling for potential confounders through propensity score analysis, the association between smoking and intraoperative blood loss remained significant. In addition, our study identified that surgical process, the number of surgical segments involved, and APTT were also linked to intraoperative blood loss. Our findings suggest that implementing smoking cessation programs, careful surgical planning, and preoperative coagulation function adjustments can significantly contribute to the prevention of intraoperative bleeding among patients with metastatic spinal tumors.

Advantages of propensity score analysis

Propensity score analysis offers several advantages in observational studies. It allows for the control of multiple confounding variables, particularly in situations where randomization is not feasible or ethical [31]. By

Table 4 Subgroup analysis of outcomes based on the smoking exposure duration

Characteristics	Overall	Smoking exposure duration			*P*
		None	Short term	Long term	
Before propensity score analysis					
n	252	164	52	36	
Blood loss (mL, median [IQR])	1820.44 [1284.71, 2565.35]	1722.32 [1265.94, 2312.19]	1843.97 [1284.71, 2565.35]	2503.13 [1739.95, 3534.96]	0.003
Intraoperative massive blood loss (no/yes, %)	187/65 (74.2/25.8)	131/33 (79.9/20.1)	38/14 (73.1/26.9)	18/18 (50.0/50.0)	0.001
Length of hospital stay (days, median [IQR])	18.00 [14.00, 25.00]	18.00 [14.00, 24.00]	20.00 [15.00, 26.00]	20.50 [17.00, 33.00]	0.076
Length of hospital stay after surgery (days, median [IQR])	14.00 [11.00, 17.25]	13.00 [11.00, 16.00]	14.50 [12.00, 20.00]	13.50 [9.00, 20.00]	0.070
After propensity score analysis					
n	132	74	31	27	
Blood loss (mL, median [IQR])	1815.00 [1310.19, 2572.20]	1703.41 [1277.81, 2124.82]	1835.23 [1284.71, 2579.04]	2665.21 [1770.57, 3534.96]	0.007
Intraoperative massive blood loss (no/yes, %)	98/34 (74.2/25.8)	63/11 (85.1/14.9)	22/9 (71.0/29.0)	13/14 (48.1/51.9)	0.001
Length of hospital stay (days, median [IQR])	19.00 [14.00, 26.00]	19.00 [14.00, 26.00]	19.00 [15.00, 26.00]	18.00 [13.00, 23.00]	0.940
Length of hospital stay after surgery (days, median [IQR])	13.00 [9.75, 16.00]	13.00 [10.00, 16.00]	14.00 [12.00, 20.00]	11.00 [9.00, 14.00]	0.069

IQR, Interquartile range

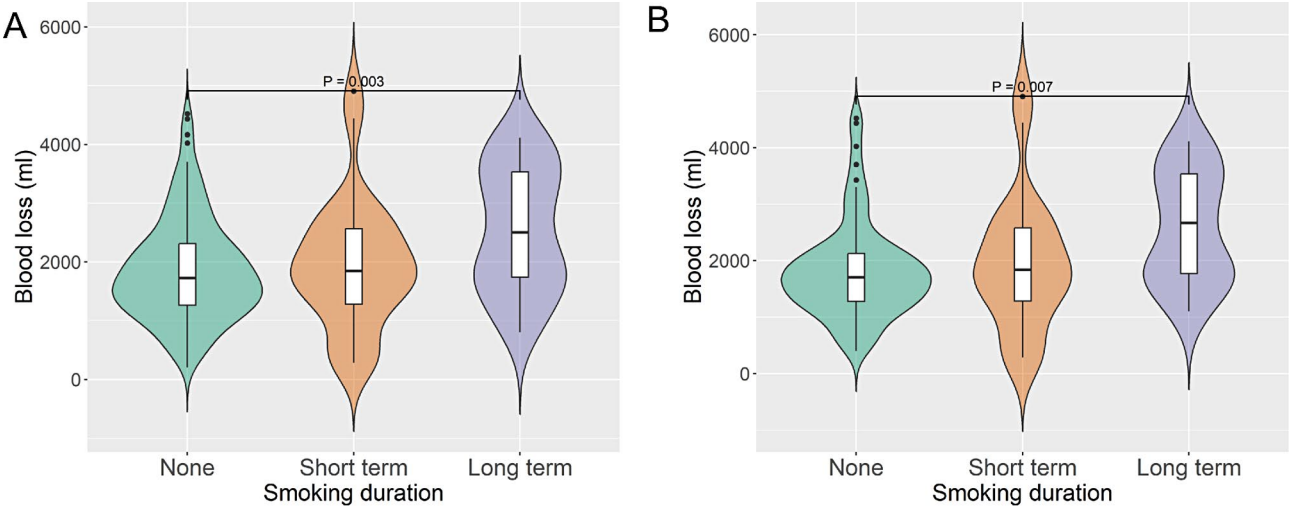

Fig. 3 Violin plot for the distribution of intraoperative blood loss based on smoking duration. (**A**) Before propensity score matching analysis; (**B**) After propensity score matching analysis

using propensity scores to match or stratify individuals with similar propensities for the exposure of smoking, the analysis could effectively balance the distribution of confounders between smoking and non-smoking groups, reducing selection bias and enhancing the comparability of the two groups. Additionally, propensity score analysis provided a flexible framework for incorporating a large number of covariates into the analysis, which can improve the precision of estimated smoking exposure effects [32]. This approach also offers transparency in the adjustment for confounding, aiding in the interpretation and communication of study results [32]. Thus, the results from our study would be compelling.

Comparison with previous studies

A study which was conducted by Nordestgaard et al. [19] investigated the potential association between smoking and surgical bleeding, as indicated by blood transfusion, in various surgical procedures, including orthopedic surgery, plastic surgery, and general surgery. Utilizing data from the American College of Surgeons National Surgical Quality Improvement Program, the study analyzed over 5 million cases from 680 hospitals across the United States. The results showed that smokers had a higher risk of receiving transfusions and surgical bleeding, with odds ratios of 1.06 for both smokers and nonsmokers. Additionally, cumulative smoking was found to increase the odds ratios significantly. However, smoking did not increase the risk of reoperations due to bleeding

Table 5 Multiple linear analysis of clinical characteristics for the amount of intraoperative blood loss before and after propensity score analysis

Characteristics	Propensity scores matching analysis			
	Before		After	
	Estimate	*P* value	Estimate	*P* value
(Intercept)	-0.541	0.770	0.578	0.854
Smoking				
No	Ref.		Ref.	
Yes	1.410	0.001	1.443	0.010
Primary tumor type				
Slow	Ref.		Ref.	
Moderate	-0.093	0.840	0.932	0.223
Rapid	-1.225	0.007	-0.644	0.446
Age	0.008	0.658	-0.029	0.355
Gender				
Male	Ref.		Ref.	
Female	0.241	0.583	-1.158	0.410
BMI	-0.066	0.086	-0.091	0.209
Diabetes				
No	Ref.		Ref.	
Yes	0.169	0.745	0.989	0.338
Hypertension				
No	Ref.		Ref.	
Yes	0.231	0.566	1.250	0.065
Preoperative chemotherapy				
No	Ref.		Ref.	
Yes	-1.096	0.041	-1.456	0.182
Extravertebral bone metastasis				
No	Ref.		Ref.	
Yes	-0.539	0.156	0.301	0.650
Visceral metastases				
No	Ref.		Ref.	
Yes	0.021	0.964	-0.040	0.961
KPS				
> 50	Ref.		Ref.	
≤50	0.216	0.585	-1.038	0.144
Preoperative embolization				
No	Ref.		Ref.	
Yes	-0.408	0.597	-1.561	0.199
Surgical process				
Palliative decompression	Ref.		Ref.	
Partial resection of vertebrae	1.441	0.034	-0.517	0.789
En bloc resection of vertebrae	1.506	0.042	3.321	0.009
Surgical site				
Cervical and cervical thoracic	Ref.		Ref.	
Thoracic and thoracolumbar	0.223	0.776	0.356	0.777
Lumbar and lumbosacral	0.763	0.364	1.797	0.210
Number of surgical segments				
1	Ref.		Ref.	
≧2	0.851	0.027	1.836	0.017
Hypoalbuminemia				
No	Ref.		Ref.	
Yes	-0.219	0.685	-0.321	0.697
Thrombocytopenia				
No	Ref.		Ref.	

Table 5 (continued)

Characteristics	Propensity scores matching analysis			
	Before		After	
	Estimate	*P* value	Estimate	*P* value
Yes	-15.088	0.986	-14.605	0.991
PT				
<12	Ref.		Ref.	
≥12	0.428	0.317	0.929	0.242
APTT				
<32	Ref.		Ref.	
≥32	1.110	0.008	1.435	0.045

BMI, Body mass index; KPS, Karnofsky performance status; Ref., References; PT, Prothrombin time; APTT, Activated partial thromboplastin time

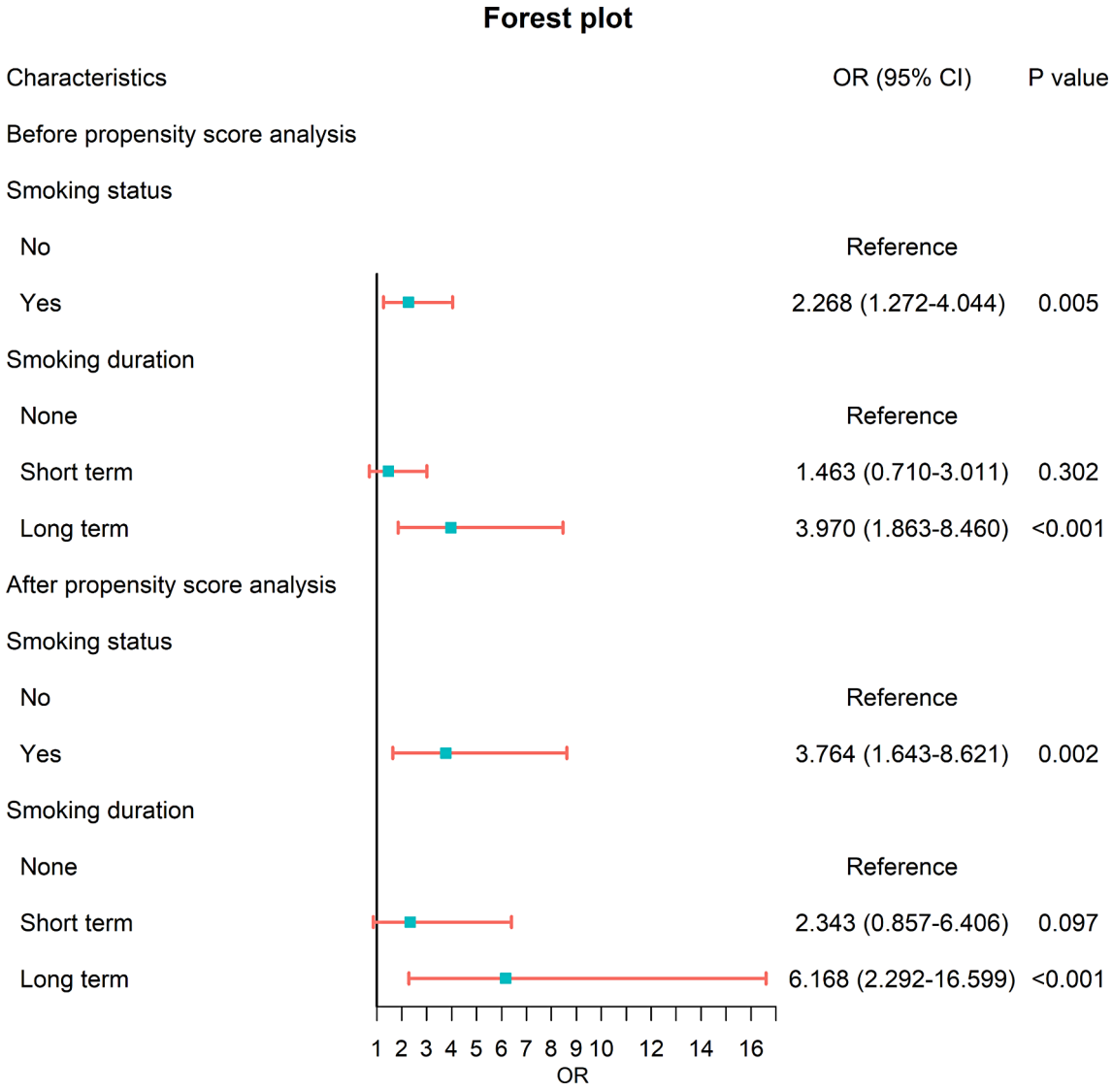

Fig. 4 Forest plot for the odds ratio of intraoperative massive blood loss in terms of smoking status and smoking duration before and after propensity score matching analysis. OR, odds ratio; CI, confident interval

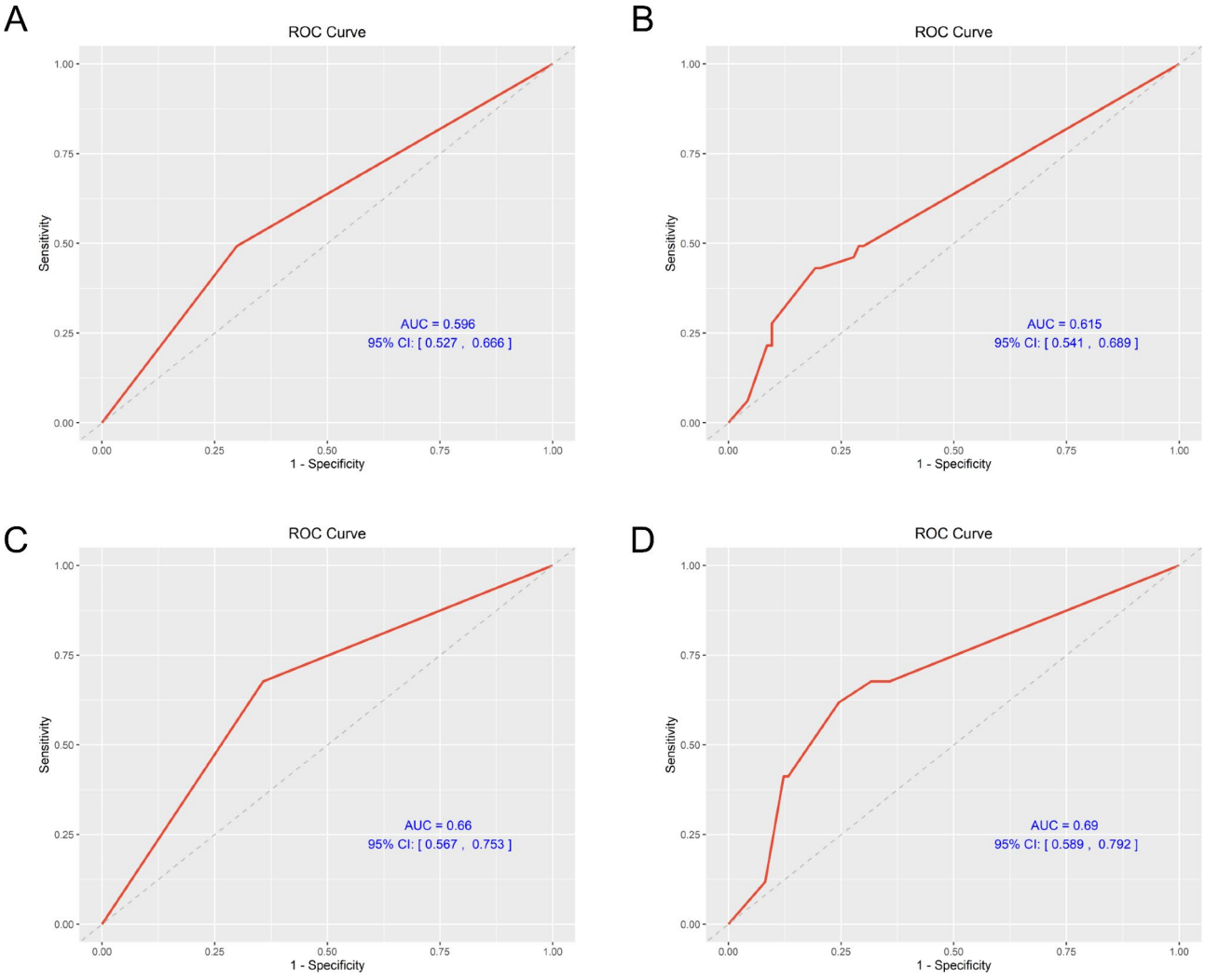

Fig. 5 Area under the receiver operating characteristic curve analysis of smoking for predicting intraoperative massive blood loss. (**A**) Smoking status before propensity score matching analysis; (**B**) Smoking duration (in years) before propensity score matching analysis; (**C**) Smoking status after propensity score matching analysis; B. Smoking duration (in years) after propensity score matching analysis

specifically. Another study by McCunniff et al. [17] found that smokers had significantly more blood loss and a higher incidence of transfusion use than non-smokers in patients undergoing lumbar spinal surgery. To provide further details, the study revealed that smokers had a higher estimated blood loss than nonsmokers, with a difference of 328 mL. In our study, before conducting propensity score matching analysis, smokers were found to have a higher intraoperative blood loss of 216 mL compared to nonsmokers, which was similar to the above study. After propensity score matching analysis, this value increased to 390 mL, indicating that smoking has a significant impact on inducing intraoperative bleeding.

Mechanisms of increased blood loss due to smoking

Cigarette smoke is a complex mixture containing thousands of harmful chemicals, including nicotine, tar, carbon monoxide, formaldehyde, benzene, ammonia, hydrogen cyanide, and heavy metals [33]. These components contribute to serious health risks and a range of complex biological effects. Studies have shown that smoking facilitated the recruitment of inflammatory cells to the walls of blood vessels and stimulated the release of various oxidative agents. This increase in inflammation, coupled with elevated levels of free radicals [34], ultimately led to the degradation of endothelial cells and inflicted damage upon the vessel walls [35]. Additionally, the heightened shear stress experienced by the endothelium, caused by increased blood viscosity and altered hemodynamic forces, further aggravated this damage. As a result, the weakened condition of the vessel walls made them more vulnerable to rupture and bleeding, especially during surgical interventions. In addition, several other studies have shown that smoking was

able to cause vasoconstriction, impair platelet function, and increase the risk of bleeding disorders, all of which could contribute to increased blood loss [36, 37]. Furthermore, smoking has been associated with an increased risk of wound infections and delayed healing [36], possibly because smoking has a long-term effect on the functions of inflammatory and reparative cells, resulting in delayed healing and increased risk of complications [37]. The detrimental effects of smoking on vascular health are multifaceted, leading to increased blood loss during surgical procedures. The compounded risks of wound infections and delayed healing further exacerbate these issues, highlighting the significant impact of smoking on surgical outcomes and recovery. Hence, addressing smoking cessation is crucial for improving patient prognosis and minimizing surgical complications.

Identification of other potential risk factors for intraoperative blood loss

This study further sought to identify other potential risk factors for intraoperative blood loss especially among metastatic spinal tumors. Other studies have shown that large invasive surgery, such as partial or total vertebrectomy, was significantly associated with intraoperative blood loss [38, 39], which was consistent with our study. Because our findings revealed that surgical process with large invasive surgery, and a higher number of surgical segments were associated with more intraoperative blood loss. In the present study, our also found that APTT was significantly relevant to intraoperative blood loss, indicating the importance of adjusting coagulation function before and during surgery for metastatic spinal tumors. Additionally, other studies have indicated that intraoperative changes in mean arterial pressure (MAP) [40, 41] and the use of hemostatic agents [42] were closely linked to the volume of intraoperative blood loss. It is important to emphasize that our research focused specifically on investigating the causal relationship between smoking and intraoperative massive blood loss. However, intraoperative blood loss can also significantly impact the stability of MAP. Namely, the interplay between intraoperative blood loss and MAP is more complicated than the unidirectional and casual relationship observed between smoking and blood loss in our study. Thus, a deeper examination of MAP control could shift the focus of our study, introducing a new variable that distracts from the direct causal effects of smoking on intraoperative blood loss. Moreover, fluctuations in MAP were influenced by various factors, including fluid management [43], medication administration, and patients' physiological responses. For these reasons, we have chosen not to explore the subsequent changes in MAP resulting from blood loss in our analysis. Additionally, concerning the use of hemostatic agents, we recommended administering tranexamic acid intravenously at a dose of 10 to 20 mg/kg prior to the procedure, followed by a continuous infusion at a rate of 1 mg/(kg·h), and during the surgery, utilizing a solution of 3 g of tranexamic acid dissolved in 250 ml of saline along with local tamponade techniques to effectively control bleeding after gauze infiltration for all patients with metastatic spinal disease treated with decompressive surgery [44].

Clinical implications

The findings of this study have important clinical implications for the management of patients with metastatic spinal tumors. The study has demonstrated that smoking significantly contributes to increased intraoperative blood loss in these patients. By identifying smoking as a risk factor for intraoperative blood loss, this study highlights the importance of assessing smoking status in preoperative evaluations and implementing smoking cessation interventions to minimize blood loss during surgery and improve patient outcomes. For elective surgery, a randomized clinical trial has shown that quitting smoking at least four weeks prior to surgery can significantly reduce postoperative complications in patients undergoing general and orthopedic procedures [45]. In addition, a randomized controlled study has demonstrated that smoking cessation could also effectively reduce surgical site infection [36]. For certain emergency surgeries, patients may have required immediate intervention before they could complete a smoking cessation program. We emphasized that real-time coagulation assessment was essential for managing bleeding effectively and ensuring optimal patient outcomes. In our study, we highlighted the importance of continuously monitoring coagulation parameters throughout the surgical procedure. This included employing point-of-care testing to evaluate key factors such as prothrombin time, activated partial thromboplastin time, and platelet function. By closely tracking these parameters, we were able to make well-informed decisions regarding the necessity for transfusions of platelets, plasma, or other hemostatic agents tailored to each patient's specific needs. Furthermore, the study has identified other risk factors associated with increased intraoperative blood loss, including surgery process and primary tumor type. These findings could provide valuable insights for surgical planning and decision-making, allowing for the identification of patients at higher risk for excessive blood loss and facilitating the implementation of appropriate interventions.

Limitations

There are also some limitations to our study. Firstly, while our sample size is relatively adequate for the analysis, it is important to note that the study was conducted at only two institutions in our country. This limitation may affect

the generalizability of our findings to other regions or cultural contexts. Future research should consider incorporating a more diverse range of institutions and patient demographics to enhance the applicability of the results across different populations and surgical practices. Secondly, the study categorized patients into smoking and non-smoking groups based on self-reported smoking status. However, there is a possibility of misclassification bias due to underreporting or misreporting of smoking habits by the patients. To enhance the reliability of our findings, the inclusion of biochemical verification methods, such as cotinine testing [46], could be considered in the future. Lastly, while the study identified smoking as a significant contributor to intraoperative blood loss, it did not directly provide data on the effectiveness of smoking cessation interventions in reducing blood loss. Thus, further research is needed to investigate the impact of smoking cessation programs on intraoperative outcomes in patients with metastatic spinal tumors.

Conclusions

Our study provides evidence that smoking is a significant contributor to intraoperative blood loss among patients with metastatic spinal tumors. However, smoking may not directly prolong patient's hospitalization time. Future studies are needed to explore the mechanisms underlying the association between smoking and intraoperative blood loss and to identify effective smoking cessation interventions for patients with metastatic spinal tumors.

Author contributions

All authors took part in designing and writing the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets of the current study are available under reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the research ethics board of the Peking University First Hospital, and written informed consent was obtained from all patients. Additionally, this study was conducted in accordance with the Declaration of Helsinki, and the work has been reported in line with the STROCSS criteria.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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