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ORIGINAL ARTICLE

Pre-operative embolisation of spinal tumours: neither neglect the neighbour nor blindly follow the gold standard

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Abstract

A large variety of vertebral tumours undergoes transarterial embolisation (TAE) prior to surgery. However, the subsequent intra-operative blood loss is unpredictable. This retrospective analysis, aims to determine the impact of various factors that may potentially influence the estimated intra-operative blood loss (EBL) in these patients. The study included 56 consecutive patients with spinal tumours who underwent pre-operative TAE. Demographic information, treatment history, tumour type, MRI characteristics, angiographic appearance, embolisation technique and surgical invasiveness were correlated with EBL using univariate and multivariate analysis. Mean EBL was 1317 mls. On univariate analysis, haematological/primary tumours, MRI hypervascularity and selective embolisation were significantly ($P < 0.05$) associated with increased EBL. A total angiographic devascularisation and embolisation of additional segments above and/or below the involved level were significantly associated with decreased EBL. There was no significant association with hypervascular angiographic appearance or surgical invasiveness. MRI and angiographic hypervascularity were not entirely concordant, especially for the category of moderately vascularised metastases. After multivariate analysis, MRI hypervascularity (1434 vs. 929 mls, $P = 0.018$) and embolisation of additional segments (1082 vs. 1607 mls, $P = 0.003$) remained significantly correlated with EBL. In conclusion, during pre-operative TAE of spinal tumours, routine angiographic interrogation of additional levels above and below the involved segment should be made, with a low threshold for embolising them, if safely performable. Compared to angiographic gold standard, MRI hypervascularity is probably a better predictor of EBL.

Keywords Transarterial embolisation of spinal tumours · Spinal tumour · MRI of vertebral metastasis · Angiography for vertebral metastasis · Intra-operative blood loss

Introduction

Spinal metastasis is present in 30–90% of patients who die from cancer, with the breast, lung and prostate being the most commonly encountered primary source of malignancy [1]. It may be symptomatic in up to 10% of cancer patients and lead to substantial morbidity [1]. Surgical stabilisation and neurological decompression can improve the quality of life in patients with spinal metastasis, but these surgeries are complex and carry risk of catastrophic intra-operative haemorrhage [2–4]. Over the past three decades, pre-operative transarterial embolisation (TAE) of spinal tumours has emerged as a valuable treatment adjunct for hypervascular metastases, and multiple case series have reinforced its value in decreasing perioperative blood loss as well as facilitating tumour resection [5–8]. It has also been employed with varying effectiveness in metastases not traditionally thought of as hypervascular, as well as for haematological and primary tumours [7, 9–11].

While a variety of tumours get embolised pre-operatively, our ability to predict the effectiveness of TAE in reducing the EBL is limited. In particular, the role of pre-operative angiographic and MRI characteristics on intra-operative blood loss and the value of embolisation in traditionally non-hypervascular metastases are under-explored. This study aims to determine the impact of various factors that may potentially

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influence intra-operative estimated blood loss (EBL) following pre-operative TAE.

Materials and methods

The study had Institutional Review Board approval. A retrospective review of the electronic medical records between 2009 and 2016, including the hospital surgical database and picture archiving and communication system (PACS), identified 56 consecutive patients who underwent embolisation prior to spinal tumour surgery.

Clinical information

Demographic information and history of prior radiotherapy to the same level were obtained. The tumours were categorised into three categories: (1) primary/haematological tumours, e.g. haemangioma, myeloma and lymphoma; (2) highly vascularised metastases (renal cell, thyroid and hepatocellular carcinoma); and (3) moderately vascularised metastases (lung, breast, prostate, gastrointestinal and other epithelial tumours). This classification of metastases was based on previously described grades of vascularity [12].

Magnetic resonance imaging

Of the 56 cases, 52 patients underwent magnetic resonance imaging (MRI) of the spine within the 4 weeks preceding surgery and had images available for review. The scan protocol included the following sequences: sagittal and axial T2-weighted fast spin echo, sagittal T1-weighted fast spin echo, and sagittal short-tau inversion recovery sequence performed on a 1.5T/3T whole body scanner. Sagittal and axial T1-weighted fat-suppressed sequences post-administration of intravenous gadolinium contrast were also routinely acquired unless there was a contraindication to gadolinium administration (such as severe renal impairment).

The MRI images were retrospectively read by two radiologists blinded to the primary tumour diagnosis and angiographic and surgical outcomes. The following features were assessed: presence of pathological compression fracture, estimated tumour volume using the prolate ellipsoid formula ($< 50\ cm^3$, $\geq 50\ cm^3$), proportion of soft tissue component ($< 50\%$, $\geq 50\%$), number of columns involved (< 3, 3) (the anterior column defined as the anterior wall of the vertebral body, the anterior longitudinal ligament and anterior annulus fibrosus; the middle column as the posterior wall of the vertebral body, posterior longitudinal ligament and posterior annulus fibrosus; and the posterior column as the posterior elements and facet joints [13]), tumour epicentre (vertebral body or paraspinal/posterior spinal) and presence of cord compression or severe lumbar spinal canal stenosis (defined as absent cerebrospinal fluid around the cauda equina [14]). In 42 patients who had post-contrast MRI scan, features of MRI hypervascularity were defined as presence of avid contrast enhancement, flow voids, intralesional haemorrhage with T1-/T2-hyperintense methaemoglobin or tortuous feeding vessels [15, 16].

Pre-operative embolisation

Under local anaesthesia with or without mild sedation, all patients underwent transfemoral embolisation within 48 h of the surgery. Selective cannulation and angiography of all possible feeding arteries were performed using 4 or 5 French diagnostic angiographic catheter, with use of coaxial microcatheters (2.4 or 2.7 French) for superselective cannulation of small feeders. Operator preference, tumour vascularity, vascular anatomy and availability determined the selection of embolic agents. Most of the procedures utilised particles (gel foam slurry and/or polyvinyl alcohol (PVA)) for distal selective embolisation, with or without adjunctive proximal coil embolisation. Proximal embolisation alone (either with coils or by flow-directed particle embolisation without selective cannulation of the feeding artery) was performed if distal embolisation was not possible or deemed unsafe, e.g. if the feeding vessel also supplied a radiculo-medullary artery. Tumoural supply from segmental arterial feeders above and/below the affected level was embolised if they were contributing to the tumour blush.

The angiographic images on PACS were retrospectively reviewed. Angiographic hypervascularity was defined as early arterial phase enhancement, hypertrophic tortuous feeding arteries and intratumoural pooling of contrast or arteriovenous shunts. Capillary phase tumoural blush was interpreted as enhancement more than neighbouring normal vertebra and not showing features of a hypervascular tumour.

The following embolisation-related features that could potentially affect the outcomes of TAE were analysed: time between embolisation and surgery (0–12 h, 13–24 h, 25–48 h), angiographic appearance (hypervascular or capillary blush), embolisation agent (gelfoam only; PVA with or without gelfoam; coils and particles), extent of embolisation (partial ($< 50\%$), subtotal (50–80%) or total ($> 80\%$)), level of embolisation (proximal or selective) and whether additional segment(s) above and/or below the affected segment were embolised.

Spine surgery

The indications for spinal surgery were neurologic deficit, spinal instability and/or intractable pain secondary to the spinal tumour. The types of surgery performed included anterior and/or posterior stabilisation with or without corpectomy in the cervical spine and posterior instrumentation and decompression or thoracolumbar corpectomy in the thoracolumbar spine. To enable comparison of the extent of surgery, using

information from operative records, the extent of surgery was determined using a previously validated invasiveness index (Mirza) taking into account the surgical approach (anterior and/or posterior) and number of vertebrae decompressed, fused or instrumented, which were further categorised into index < 7 and ≥ 7 [17].

Outcome measures

The outcome measure was EBL, which was obtained from the anaesthetist's calculations in the operative records. This is measured by adding the blood volume collected in suction bottles and weighing the wound swabs [12].

Statistical analysis

Statistical analysis was performed using SPSS statistical software (SPSS Inc., Chicago, IL, USA). Univariate analysis was performed using the two-tailed Student *t* test for categorical variables and the Spearman's rho for contiguous variables to determine the association between each variable and EBL. Multivariate analysis was performed on variables that were significant from the univariate analysis or showed some trend of association, using a type III sum of square analysis. Statistical significance was defined as $P < 0.05$.

Results

Demographic information and tumour subtypes

In the 56 patients (37 male; 19 female, age ranging from 33 to 84 years, mean age 59 years ± 11 (SD)), 18 were (32%) were highly vascularised metastases (11 renal cell carcinomas (RCCs), 6 hepatocellular carcinoma, 1 thyroid), 29 (52%) moderately vascularised metastases (16 lung, 7 breast, 3 gastrointestinal tract, 2 gynaecological, 1 prostate) and 9 (16%) haematological/primary tumours (4 myeloma, 1 lymphoma, 4 haemangiomas) (Table 1). Only 3 (5%) patients had undergone prior radiotherapy to the affected level.

Magnetic resonance imaging

There were 28 (67%) tumours that demonstrated hypervascularity on MRI (Table 2) (Fig. 1), of which 17 demonstrated avid contrast enhancement. Flow voids were seen in 8 tumours, intralesional haemorrhage in 12 tumours and hypertrophic feeding vessels in 1 tumour. Of the 38 (70%) tumours with pathological compression fractures, more than half (22 tumours) had severe (≥ 50%) loss of vertebral body height. There were 21 tumours (39%) with a large (≥ 50%) soft tissue component, with cord compression/severe spinal canal stenosis seen in 34 (63%) cases.

Table 1 Demographic information and tumour subtypes

Demographic information	*n*
Male	37
Female	19
Age	Mean age 59 years ± 11 (SD). Range 33 to 84 years
Tumour subtypes	
Highly vascularised metastases	18
- Renal cell carcinoma	- 11
- Hepatocellular carcinoma	- 6
- Thyroid	- 1
Moderately vascularised metastases	29
- Lung	- 16
- Breast	- 7
- Gastrointestinal tract	- 3
- Gynaecological	- 2
- Prostate	- 1
Haematological/primary tumours	9
- Myeloma	- 4
- Lymphoma	- 1
- Haemangioma	- 4

Pre-operative embolisation

More than half of the tumours (29, 52%) demonstrated angiographic hypervascularity (Fig. 2). Total embolisation (at least 80% reduction in tumour blush) was achieved in 32 (57%) cases. Selective embolisation could be performed in 42 (75%) cases, while in 31 (55%) cases additional segments above and/or below the tumour level were embolised. Interestingly, 52% (15/29) of tumours with angiographic hypervascularity underwent total embolisation as compared to 63% (17/27) of tumours with capillary phase blush. Meanwhile, the majority (93%, 27/29) from the former group were amenable for selective distal embolisation versus 56% (15/27) from the latter group. Particles were used more commonly, with gelfoam used in 28 (50%) cases and PVA in 10 (18%) cases. Coils were used alone or with particles in 18 (32%) cases. There were no major post-procedural complications. Most of the patients (57%) underwent surgery within 12 h of embolisation.

Correlation of tumour subtype with MRI and angiographic vascularity

The correlation between MRI and angiographic hypervascularity was extremely modest with just 15 of the 28 tumours (53.3%) hypervascular on MRI showing angiographic hypervascularity (Table 3). There was generally better concordance between these parameters for highly vascularised metastases and primary/haematological tumours, but much less so for moderately

Table 2 Estimated blood loss for all cases

Variable	*n* (%)	Estimated blood loss		
		Mean (ml)	SD	*P* value
Patient				
Age	56 (100)	1317	877	0.734[1]
Gender				0.948
Female	19 (34)	1345	990	
Male	37 (66)	1302	827	
Previous radiotherapy				0.920
No	53 (95)	1314	895	
Yes	3 (5)	1367	569	
Tumour subtype				0.037, 0.109, 0.844, 0.078[2]
Highly vascularised metastases	18 (32)	1554	961	
Moderately vascularised metastases	29 (52)	1036	518	
Haematological/primary tumours	9 (16)	1744	1327	
MRI				
MRI hypervascularity				*0.021*
No	14 (33)	929	379	
Yes	28 (67)	1434	972	
Pathological compression fracture				0.908
No	16 (30)	1350	1007	
Yes	38 (70)	1319	843	
Tumour volume				0.570
< 50 cm^3	45 (83)	1297	822	
≥ 50 cm^3	9 (17)	1483	1201	
Proportion of soft tissue component				0.670
$< 50\%$	33 (61)	1370	842	
$\geq 50\%$	21 (39)	1263	968	
Number of columns				0.065
< 3	4 (7)	2113	1809	
3	50 (93)	1266	770	
Tumour epicentre				0.386
Vertebral body	38 (70)	1397	837	
Paraspinal or posterior spinal	16 (30)	1166	1000	
Cord compression/severe spinal canal stenosis				0.222
No	20 (37)	1135	674	
Yes	34 (63)	981	168	
Angiographic				
Angiographic appearance				0.131
Capillary blush	27 (48)	1135	586	
Hypervascular	29 (52)	1485	1063	
Extent of embolisation				0.018; 0.988; 0.189; 0.026[3]
Partial	5 (9)	1740	1148	
Subtotal	19 (34)	1679	1018	
Total	32 (57)	1035	632	
Time between embolisation and surgery				0.926
0–12 h	33 (59)	1355	964	
13–24 h	19 (34)	1254	799	
25–48 h	4 (7)	1300	560	
Embolisation agent				0.435

Table 2 (continued)

Variable	*n* (%)	Estimated blood loss		
		Mean (ml)	SD	*P* value
Gelfoam	28 (50)	1164	627	
PVA or gelfoam + PVA	10 (18)	1443	943	
Coils + particles	18 (32)	1146	270	
Level of embolisation				0.039
Proximal	14 (25)	900	469	
Selective	42 (75)	1455	939	
Additional segments embolised				0.036
No	25 (45)	1607	1086	2.6
Yes	31 (55)	1082	582	1.7
Operative				
Invasiveness index (Mirza)				
All	56	1317	877	0.551[1]
< 7	24 (43)	1347	1109	0.825
≥ 7	32 (57)	1294	671	

[1] Spearman rank-order correlation

[2] *P* value from ANOVA test; statistical significance of Tukey's post hoc test between highly vascularised and moderately vascularised groups, highly vascularised and haematological groups, and moderately vascularised and haematological groups

[3] *P* value from ANOVA test; statistical significance of Tukey's post hoc test between partial and subtotal groups, partial and total groups, and subtotal and total groups

vascularised metastases. A meagre 23.1% (3/13) of MRI hypervascular moderately vascularised tumours were hypervascular on angiography.

Spine surgery

The invasiveness index for the surgery ranged from 1 to 18 (mean 8), with 32 (57%) cases belonging to the more invasive (index ≥ 7) subset [17].

Intra-operative blood loss

The association of each variable with EBL (univariate analysis) is summarised in Table 1.

There was a significant difference ($P = 0.037$) in EBL between the tumour groups, with haematological/primary tumours showing greatest blood loss (mean 1744 mls) compared to highly vascularised (1554 mls) and moderately vascularised (1036 mls) metastases.

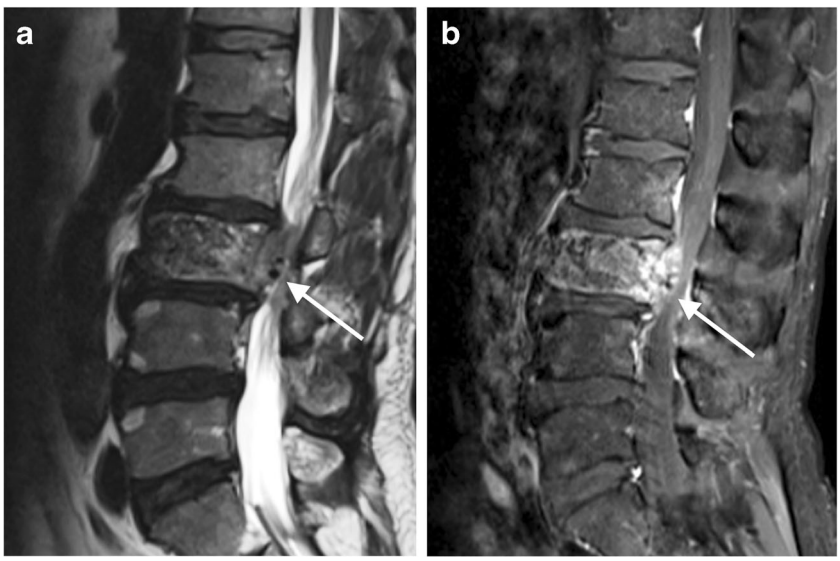

Fig. 1 Hypervascular renal cell carcinoma metastasis. **a** Sagittal T2-weighted image demonstrates a heterogeneous mass with flow voids (arrow) in L3 vertebral body, which is narrowing the spinal canal. **b** Sagittal post-contrast T1-weighted image again demonstrates the flow voids (arrow), as well as avid contrast enhancement

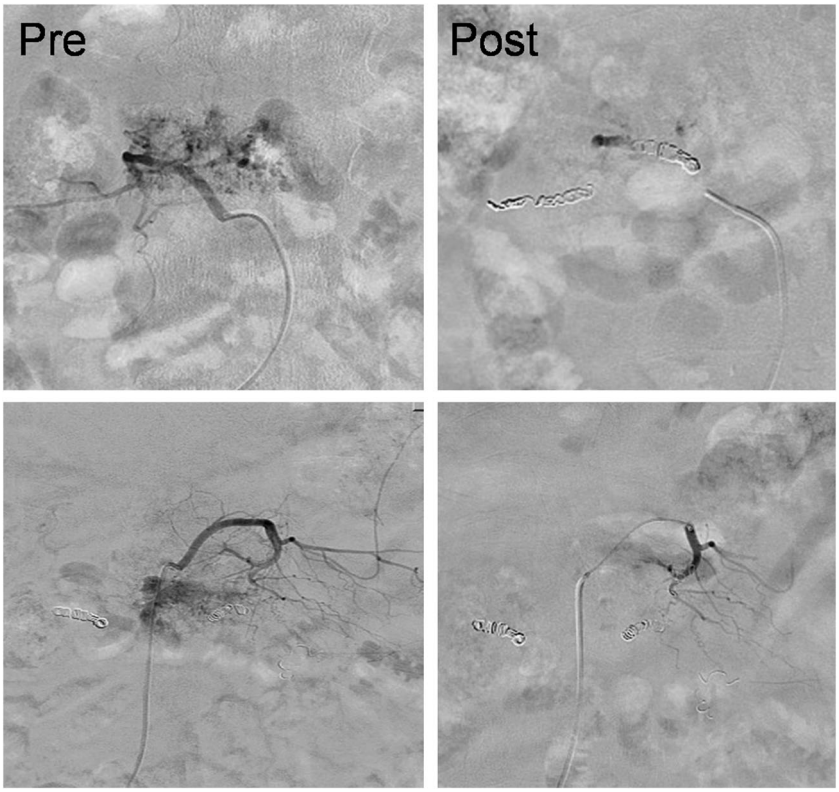

Fig. 2 Digital subtraction angiograms of the same patient as shown in Fig. 1 through selective cannulation of the segmental arteries at L3 level. Not the marked hypervascularity of the pre-embolisation images in the left column and complete devascularisation in the post-embolisation images on the right

Tumours which demonstrated hypervascularity on MRI had significantly greater blood loss (1434 vs. 929 mls, $P = 0.021$). On the contrary, there was no significant association with angiographic hypervascularity.

With regard to embolisation factors, increased extent of devascularisation ($P = 0.018$) and embolisation of additional segment(s) above and/or below the tumour level ($P = 0.036$) were associated with decreased blood loss. Selective

Table 3 Correlation of tumour subtype with MRI and angiographic vascularity

	Angiographic hypervascularity present	Angiographic hypervascularity absent	Total
MRI hypervascularity present	A[1] = 8	A = 2	A = 10
	B[2] = 3	B = 10	B = 13
	C[3] = 4	C = 1	C = 5
	Total = 15	Total = 13	Total = 28
MRI hypervascularity absent	A = 2	A = 2	A = 4
	B = 4	B = 6	B = 10
	C = 0	C = 0	C = 0
	Total = 6	Total = 8	Total = 14
Total	A = 10	A = 4	Sensitivity[4] 71.4%
	B = 7	B = 16	Specificity 38.1%
	C = 4	C = 1	Positive predictive value 53.6%
	Total = 21	Total = 21	Negative predictive value 50%

[1] Highly vascularised metastases

[2] Moderately vascularised metastases

[3] Haematological/primary tumours

[4] Of MRI hypervascularity in predicting angiographic hypervascularity

embolisation ($P = 0.039$) was associated with greater blood loss. There was no significant association with the type of embolisation agent, time between embolisation and surgery or invasiveness index of the surgery.

After multivariate analysis, MRI hypervascularity ($P = 0.018$) and additional segment(s) embolised ($P = 0.003$) remained significantly associated with increased and decreased EBL respectively (Table 4).

Discussion

Total embolisation of the spinal tumour was achieved in 57% of cases, slightly lower than a recently published meta-analysis of 37 studies (68.3%) [18]. This may be partly due to the smaller proportion of tumours with angiographic hypervascularity in our study. In the absence of a dominant hypertrophic artery, selective distal cannulation and embolisation is not feasible. There were no major procedural complications, consistent with the low rates (3.1%) reported in the literature [18]. Haematological/primary tumours had the highest EBL. Almost half of these had multiple myeloma (four out of the nine cases). The mean EBL of the myelomatous tumours (2163 mls) was higher than the other tumours. It has been previously reported that myeloma is less amenable to TAE as its vascularity is derived from fine capillary networks rather than large segmental feeders [16]. Besides, these patients were on bortezomib, a second-line treatment for multiple myeloma, which is associated with platelet dysfunction [19, 20]. Although there was a stepwise decrease in blood loss with more comprehensive angiographic devascularisation, it was not significant at multivariate analysis as reported in several studies before [6, 9, 10, 21].

There was significantly lower EBL when segmental arteries above and/or below the spinal level affected were embolised. This variable has not been widely investigated in previous studies. Wilson et al. found less blood loss with embolisation of additional segments, especially for RCCs, although this did not reach statistical significance [9]. Embolisation of additional segments may confer further benefit in reducing EBL as tumours can parasitise blood supply from adjacent segments and contribute to substantial haemorrhage [22, 23]. We therefore recommend routine interrogation of segments above and below the level of tumour involvement, and a low threshold in performing embolisation even in the presence of minor tumoural supply from such sources. However, this should be balanced with the potential risks of non-target embolisations and complications such as delayed wound healing and post-embolisation pain.

We observed significantly higher EBL in patients with MRI hypervascularity while angiographic hypervascularity was not meaningful in this respect. The latter has been documented before [7, 21, 24] while the former is a less-explored finding. The extent of contrast enhancement on MRI is an interplay of multiple factors, including the rate of intravascular contrast delivery (degree of neoangiogenesis) and the amount of contrast extravasation into the interstitial space (capillary permeability) [25]. Meanwhile, angiographic hypervascularity is usually a function of blood supply through hypertrophied tumoural feeders that can be selectively cannulated to perform an angiogram. Hence, routine contrast-enhanced MRI may be a better representative of the blood supply from the innumerable tiny arterial feeders that cannot be selectively interrogated with angiography. This could be the cause for the cases of MRI hypervascularity without angiographic hypervascularity seen in our study. Similar finding has been reported previously [10, 16]. The rate of total embolisation was also lower in tumours demonstrating MRI hypervascularity (54% (15/28) vs. 71% (10/14)), possibly contributing to the better correlation between MRI hypervascularity and increased EBL. This brings forth the need for exploring alternative techniques beyond the endovascular route to deliver the embolic agent into the tumoural capillary bed. A direct percutaneous injection of embolic agents such as glue or Onyx (ev3, Irvine, California) into the tumour could be a solution. This has emerged as a routine adjunct or alternative to pre-operative transarterial embolisation for hypervascular head and neck tumours [26]. There are anecdotal reports of pre-operative embolisation of vertebral tumours through direct puncture [27–29]. The better predictability of blood loss based on MRI also highlights the value of gadolinium-enhanced scans in these patients. In the present era, when there is an increasing tendency to reduce the use of gadolinium-based contrast

Table 4 Multivariate analysis for estimated blood loss

Variable	DF	Sum of squares	Mean square	*F* statistic	*P* value
Tumour subtype	2	437,162.167	218,581.084	0.419	0.661
MRI hypervascularity	1	3,237,864.892	3,237,864.892	6.200	0.018
Number of columns	1	661,907.959	661,907.959	1.267	0.268
Level of embolisation (proximal vs. selective)	1	1,168,292.669	1,168,292.669	2.237	0.144
Additional segments embolised	1	5,296,745.044	5,296,745.044	10.142	0.003

R squared = 0.386 (adjusted R squared = 0.280)

media (due to its unpredictable long term side effects), this finding can be a reasonable justification to perform contrast-enhanced MRI prior to spinal tumour surgery.

There was no correlation of EBL with the invasiveness or extent of surgery as defined by the Mirza index. This was unlike earlier studies by Kobayashi and Robial et al., which found more blood loss for more invasive surgery [11, 21]. However, the reliability of this observation needs to be tested through matched comparison with tumours that had undergone surgery of similar invasiveness without pre-operative embolisation. Until then, it is reassuring to accept our observation which suggests that with adequate pre-operative embolisation, more invasive spinal surgery can be performed without unduly increasing the EBL.

Our study has several limitations with its retrospective nature being the foremost. Unlike some other studies, we only evaluated EBL and did not include blood transfusion as an outcome variable. Blood transfusion is affected by several considerations outside of intra-operative blood loss, such as surgeon or anaesthetist's preference, patient's comorbidities and local practices. While we have analysed the impact of several factors that could potentially affect the blood loss, there may be others we have not accounted for, e.g. differences in surgical hardware and techniques, epidural venous bleeding and extent of soft tissue resection.

In conclusion, pre-operative spinal tumour embolisation should not be restricted to TAE through the dominant feeders from the primary segmental artery. Neighbouring arteries that could supply the tumour should be thoroughly interrogated and embolised if required. MRI hypervascularity correlates poorly with the traditional gold standard of angiographic hypervascularity, especially in moderately vascularised metastases. Since MRI hypervascularity is a better predictor of higher EBL, operative planning should probably be based on MRI appearance instead of angiographic one. In tumours with MRI hypervascularity without angiographic hypervascularity or with difficulty in achieving comprehensive devascularisation, there may be a need to explore alternative embolisation techniques (e.g., direct percutaneous injection) beyond the conventional transarterial ones.

Compliance with ethical standards

Conflict of interest The author declares that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

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