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Blood Loss in Surgery for Aggressive Vertebral Haemangioma with and without Embolisation

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Despite their benign nature some symptomatic aggressive vertebral haemangiomas (AVH) require surgery to decompress spinal cord and/or stabilise pathological fractures. Preoperative embolisation may reduce the considerable blood loss during surgical decompression. This systematic review investigated whether preoperative embolisation reduced surgical blood loss during treatment of symptomatic AVH. PubMed Medline, Web of Science, and Ovid Medline were searched for case reports and clinical studies on surgical AVH treatment. Included were cases from all publications on surgical treatment of AVH where the amount of surgical blood loss and the use of preoperative embolisation were documented. 51 cases with surgically treated AVH were retrieved from the included studies. Blood loss in the embolised treatment group (980±683 mL) was lower than the non-embolised control group (1,629±946 mL). This systematic review found that embolisation prior to AVH resection reduced surgical blood loss (level of evidence, very low) and can be recommended (strong recommendation).

Keywords: Spinal cord compression; Hemangioma; Therapeutic embolisation; Surgical blood loss

Introduction

Aggressive vertebral haemangiomas (AVH) are benign vascular tumours, which breach the posterior cortical wall of the affected vertebra, may affect anterior column stability, and compress the spinal cord epidurally [1]. Due to the benign nature of the tumour, metastatic spreading does not occur, but impaired vertebral stability or myelopathy may require surgical treatment for stabilisation and decompression [2]. A representative case is presented in Fig. 1.

Depending on the affected vertebral level and the anterior and posterior extent of the lesion, there are combined surgical accesses to decompress and stabilise AVH. Due to high vascularisation of haemangiomas, copious bleeding may complicate surgery, and can even be life-threatening [1].

Embolisation of spinal tumours *via* flouroscopically-controlled endovascular intervention aims at choking off the blood flow in the tumour by blocking the feeding arteries, and thus reducing surgical blood loss. Many substances can be used for embolisation depending of the size of the vessel and the desired length of occlusion [3]. Liquid embolic agents (i.e., Onyx) [4], sclerosing agents (i.e., ethanol) [5], particulate embolic agents (i.e., polyvinyl ethanol) [6], and mechanical occlusion devices (i.e., coils) are commonly used as embolising agents.

Yet, many spinal interventionalists fear the possibility

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of ischaemic spinal cord injury as a complication of the embolisation procedure due to accidental occlusion of unrecognised radiculomedullary arteries. Surgeons might therefore avoid performing embolisation and rather treat bleeding surgically. Possible complications of spinal tumour embolisation are (1) emboli washout with vascular occlusion (i.e., spinal cord ischaemia, stroke, myocardial infarction, peripheral arterial occlusion) [7], (2) bleeding due to early revascularisation caused by rapid enzymatic degradation of the embolisation agents (i.e., gelfoam) [8],

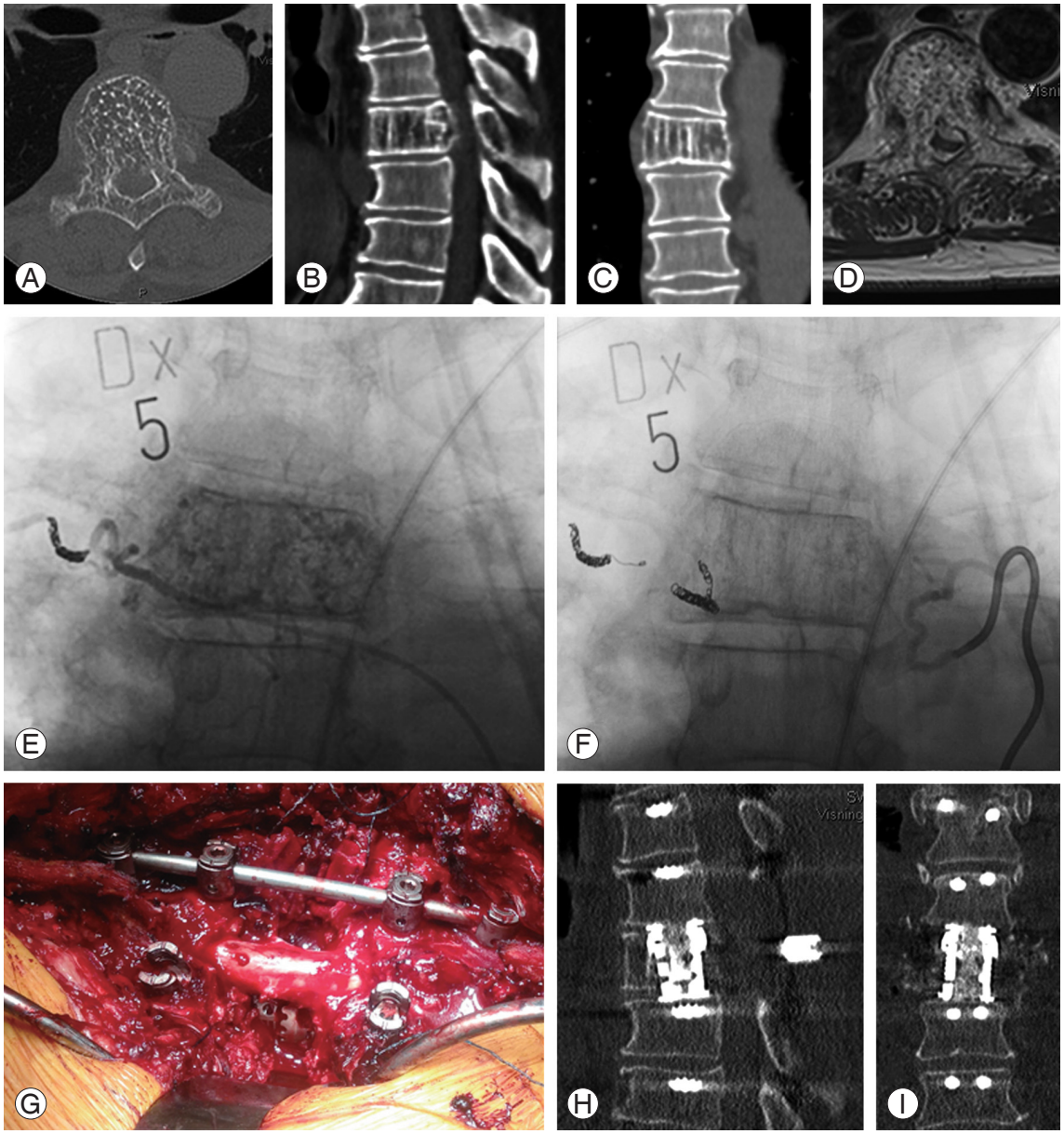

Fig. 1. Representative case of a 64-year-old man with progressive myelopathy below T6 (ASIA C). **(A–C)** Computed tomography (CT) scans revealed vertical striations on the T6 vertebral body, highly suggestive of haemangioma. **(D)** T1 magnetic resonance imaging with gadolinium contrast highlighted the epidural portion of the tumour. **(E)** After placement of the first coil, the haemangioma was still highly vascularised. **(F)** The second coil successfully occluded the feeding arteries. **(G)** The tumour was stabilised by posterior instrumentation of T4–T8, the posterior portion of the haemangioma was resected, and the vertebral body was replaced by an expandable titanium cage and autologous bone-graft. The amount of bleeding was 2,060 mL, and 550 mL red blood cell concentrate was autotransfused from the cell saver. No allogeneic blood transfusion was required. **(H, I)** Postoperative CT scans showed proper decompression and adequate stabilisation. The patient recovered completely from myelopathy within two months (ASIA E). ASIA, American Spinal Injury Association classification.

and (3) allergic reactions to the embolising agents [9].

Kobayashi et al. [7] reviewed 62 patients who underwent preoperative embolisation of spinal tumours. In their cohort, the degree of embolisation itself did not have any significant effect on perioperative blood loss, but surgical invasiveness did (p<0.001). Therefore, the impact of preoperative embolisation should be questioned and its benefits should be weighed against possible harms. Until now, a meta-analysis of the effect of embolisation on surgical bleeding in the published case reports and case series on AVH has not been performed. This review will summarise the weak evidence for treatment of AVH, present a meta-analysis of bleeding related to the use of embolisation prior to surgery, and assess whether preoperative embolisation reduces blood loss during resection and/or decompression of symptomatic aggressive vertebral haemangioma.

Materials and Methods

This systematic review was registered in the PROSPERO database (CRD42014008862). On March 7th, 2014, a literature search was performed with PubMed Medline, Web of Science, and Ovid Medline using the search terms "(aggressive OR spinal cord) AND (spinal OR vertebral) AND haemangioma".

Limits were set to publications since 1990. The PubMed Medline search was limited to "[Title/Abstract]", and the Ovid Medline search was limited to "title".

Titles and abstracts were obtained from the respective search engines. All full-texts could be obtained from the university libraries or from openly accessible publications.

Only studies on extradural thoracic and lumbar aggressive haemangiomas were included since embolisation of cervical haemangioma is relatively contraindicated.

Case reports of AVH becoming symptomatic during pregnancy were excluded since embolisation is contraindicated in these patients due to the possible harm to the unborn. The case presented in this study was also included. The amount of bleeding (mL) was defined as the primary outcome.

The data was treated as a between-group design with two independent groups; one treatment group (embolisation) and one control group (no embolisation). The reported means, standard deviation, and number of participants in the included studies were used to compute the means, standard deviations, and number of participants in the treatment and control groups, respectively. Sample sizes were taken into account when calculating the two groups' means by calculating the weighted means. The standard deviations of the treatment and control groups were calculated by first computing the sum of squares. In a subsequent step, the sum of squares was used to calculate the variances and the standard deviations. The means, standard deviations, and number of participants in the two groups were submitted to an independent samples t-test. The effect size was calculated as Cohen's d. If not indicated otherwise, values are presented as mean±standard deviation.

Subgroup analysis was not performed and heterogeneity was not assessed. Due to the low quality of evidence and the fact that only case reports were available, sensitivity analysis was not performed.

Two authors assessed the risk of bias of included studies separately according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group guidelines for assessing risk of bias [10]. All included studies were case reports and case series; thus, both selection bias and reporting bias can be assumed. The strength of evidence was estimated and recommendations were given using the GRADE guidelines [11].

Results

The electronic search retrieved 399 publications that were screened by two co-authors. Among these, 54 publications were potentially eligible for inclusion. After full-text review, 18 publications were included (Fig. 2). While checking for outliers, the case report by Alexander et al. [2] was excluded because the value in a single participant was more than 6 standard deviations away from the mean of the control group. All 17 included studies were case reports or case series. No comparative study was included. Twelve out of the 17 included studies were single case reports.

Among the 51 included patients, 32 were females. The mean patient age was 44±19 years (range, 9–77 years). Also, 83% of AVH involved the thoracic spine.

Various types of interventions were used in the included studies. They varied from posterior decompression and vertebroplasty to circumferential *en-bloc* spondylectomy and stabilisation. Despite the fact that the different procedures are not equivalent with regard to invasiveness of the approach, selection was not performed in this context.

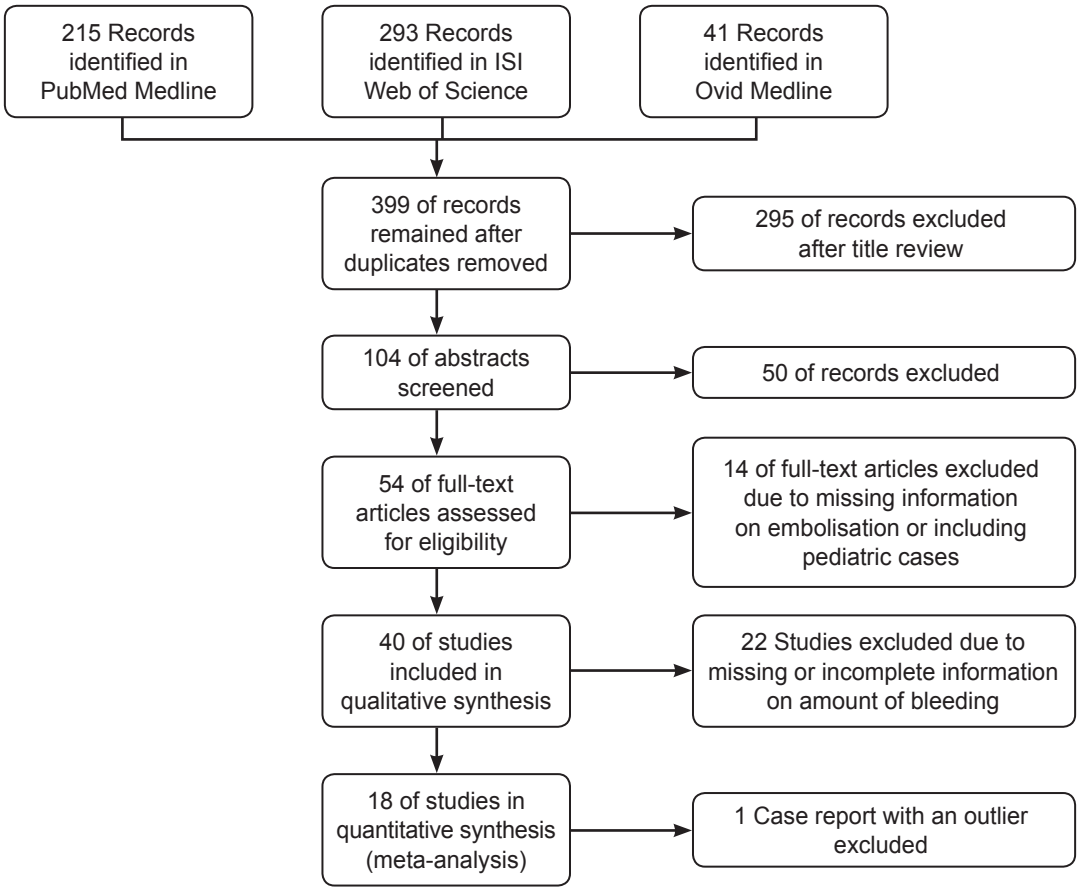

Fig. 2. Study flow diagram.

The postoperative neurological outcomes were generally positive in the published cases, irrespective of the surgical method. Only one out of the 51 cases did not show postoperative improvement (Table 1) [12-25].

The analysis indicated that there was a significant difference in the amount of blood loss between the treatment group and the control group (t [49]=2.59; p=0.013; 95% CI, 143–1,048; d=0.73). Patients in the embolised treatment group (980±683 mL) bled less than patients in the non-embolised control group (1,629±946 mL). The analysis suggests that embolisation causes reduction in bleeding during surgery.

Discussion

The available literature supports the use of preoperative embolisation in cases of AVH. The variability in effectiveness of embolisation is well reflected in these results. Embolisation does not seem to be the only factor contributing to reduction in bleeding; other factors such as surgical technique, proper anaesthesia (i.e., using low positive end-expiratory pressure), and clotting capacity of the patients also play an important role, thus diminishing the overall effect of embolisation.

With regard to spinal surgery, the amount of surgical bleeding could be related to morbidity and mortality in the postoperative course [26]. Not only transfusion risks but also cardiovascular and pulmonary complications increase with greater blood loss [27].

Preoperative embolisation is a relatively safe procedure and reported complications are rare. Other than the transient post-embolisation syndrome with low-grade fever, pain, nausea, vomiting, and an elevated white blood cell count, serious adverse events due to accidental vascular occlusion are limited to anecdotal case reports [3].

The quality of evidence is very low. Seventeen studies were included, and all studies were either case reports or case series (Table 2). With an increase in the size of AVH, the surgeon may be more inclined to use preoperative embolisation. Blinding was not performed in the included

Table 1. Characteristics of studies

Study	Design	Gender/ age (yr)	AVH level	Preoperative neurology	Interventions	Embolisation	Radiotherapy (Gy)	Bleeding (mL)	Neurology at follow-up
Yazici et al. [12] 1996	CR	Male/42	T5	Frankel D	Anterior-only decompression and fusion	Yes	-	350	Frankel E
Lee and Hadlow [18] 1999	CR	Male/63	T10	Frankel C	Anterior-only corpectomy and stabilisation	No	40	500	Frankel E
Ogura et al. [13] 2002	CR	Female/68	T11	Frankel E (pain, numbness right leg)	Posterior-anterior decompression and fusion	Yes	-	658	Improvement of back pain and numbness
Templin et al. [14] 2004	CR	Female/61	T10	Frankel E (hyperreflexia, diffuse numbness in lower extremities)	Anterior-only corpectomy	No	-	2,000	Frankel E
Ahn et al. [15] 2005	CR	Female/64	L4	Claudication, cauda equina syndrome	Posterior decompression followed by open vertebroplasty	No	-	100	Complete relief of neurologic symptoms
Dickerman and Bennett [16] 2005	CR	Male/37	T12	Pain, numbness S2–S4	Anterior-only corpectomy and stabilisation	Yes	-	250	Neurologically intact
Sakanishi et al. [17] 2006	CR	Female/67	T8	Frankel D	Posterior-anterior decompression and stabilisation	Yes	-	830	Frankel E
Inoue et al. [19] 2007	CR	Male/31	L2	Frankel E (low back pain, sensory disturbances L2 dermatome)	One stage anterior-posterior spondylectomy	Yes	-	4,000	Frankel E
Hurley et al. [4] 2008	CS	Female/41 Male/29	L2 T8	Frankel C Frankel E (back pain)	I. Staged posterior-anterior decompression and stabilisation, II. Anterior-only decompression and stabilisation	Yes	-	100 1,500	
Sucu et al. [20] 2010	CR	Male/45	T4	Frankel B	Anterior-only corpectomy	no	-	6 Units of blood (approx 3,000)	Frankel D
Kato et al. [21] 2010	CS	Male/51 Female/57 Male/48 Female/64	T6 T4 T9 T3	JOA 9.5 JOA 5.5 JOA 7 JOA 1	All patients received spondylectomy procedures	Yes	-	1,580 2,380 3,400 2,210	JOA 10.5 JOA 10.5 JOA 10.5 JOA 6.5
Gnanalingham et al. [6] 2010	CS	Male/24 Male/53	L1 L4	Frankel D Claudication	Posterior decompression, stabilisation and open vertebroplasty	Yes	-	150 200	Frankel E Hip weakness left

(Continued to the next page)

Table 1. Continued

Study	Design	Gender/ age (yr)	AVH level	Preoperative neurology	Interventions	Embolisation	Radiotherapy (Gy)	Bleeding (mL)	Neurology at follow-up
Acosta et al. [22] 2011	CS	Male/51 Female/66 Female/31 Female/26 Female/66 Male/27 Female/71 Female/55 Male/57 Male/73	T10 T3 T10 T11 T8 T4 T12 T3 T4 T4	Myelopathy Myelopathy Myelopathy Myelopathy Myelopathy Pain Pain Pain Pain Myelopathy	All patients were treated with anterior-posterior spondylectomy and stabilisation	Yes	-	1,400 500 900 2,100 1,700 1,800 1,400 300 2,800 800	Normal motor strength in all patients
Singh et al. [5] 2011	CS	Female/14 Female/20 Male/33 Female/68 Female/31 Male/14 Female/16 Female/9 Female/45 Female/10	T8 T3 T8 T9 T4 T5 T4 T5 L1 L1	ASIA-A ASIA-B ASIA-C ASIA-C ASIA-C ASIA-C ASIA-C ASIA-A ASIA-C ASIA-C	Posterior decompression and stabilisation	Yes	-	200 240 340 360 460 300 400 200 220 240l	ASIA-D ASIA-D ASIA-E ASIA-E ASIA-D ASIA-E ASIA-E ASIA-D ASIA-E ASIA-D
Song et al. [23] 2012	CS	2 Male, 7 Female/ median age, 33.6 (14–77)		1 Frankel A, 3 Frankel B, 3 Frankel C, 2 Frankel D	Posterior *en bloc* spondylectomy in all cases	No	-	1,800 (1,000–5,000)	Improvement of 1 to 3 Frankel grades
Dang et al. [24] 2012	CR	Female/41	T5	Frankel E (but back pain, thoracic radiating pain and thoracic numbness)	Posterior-only decompression with laminectomy and vertebroplasty	No	30	1,000	Frankel E
Yao and Malek [25] 2013	CS	Male/53 Female/76 Female/33 Female/74	T7 T10 T2 T6	JOA 11 JOA 10 JOA 10 JOA 7	2 Cases anterior-only, 2 cases with posterior decompression and stabilisation	Yes	-	2,200 1,400 500 900	JOA 17 JOA 16 JOA 17 JOA 11

f/u, follow-up; CR, case report; CS, case series; JOA, Japanese Orthopaedic Association score; ASIA, American Spinal Injury Association classification.

Table 2. Bleeding with vs. without embolisation

Study	Embolisation (mL)			Control (mL)		
	Mean	Standard deviation	n	Mean	Standard deviation	n
Yazici et al. [12] 1996	350	0	1	0	0	0
Lee and Hadlow [18] 1999	0	0	0	500	0	1
Ogura et al. [13] 2002	658	0	1	0	0	0
Templin et al. [14] 2004	0	0	0	2,000	0	1
Ahn et al. [15] 2005	0	0	0	100	0	1
Dickerman and Bennett [16] 2005	250	0	1	0	0	0
Sakanishi et al. [17] 2006	830	0	1	0	0	0
Inoue et al. [19] 2007	1,000	0	1	0	0	0
Hurley et al. [4] 2008	800	990	2	0	0	0
Sucu et al. [20] 2010	0	0	0	3,000	0	1
Kato et al. [21] 2010	2,393	755	4	0	0	0
Gnanalingham et al. [6] 2010	175	35	2	0	0	0
Acosta et al. [22] 2011	1,370	769	10	0	0	0
Singh et al. [5] 2011	296	91	10	0	0	0
Song et al. [23] 2012	0	0	0	1,800	1,000	9
Dang et al. [24] 2012	0	0	0	1,000	0	1
Yao and Malek [25] 2013	1,250	733	4	0	0	0
Total	980	683	37	1,629	946	14

case reports. Not all studies reported the amount of bleeding, and 36 studies were excluded due to incomplete data.

A significant publication bias must be assumed since case reports are published only if they present a rare and unique entity. Cases with incomplete radiographic examinations, suboptimal outcome, or missing documentation are often not publishable.

Only selected databases were searched using a rather conservative search string. Studies published before 1990 were not included in the study. Therefore, there is a possibility that not all studies were identified.

Conclusions

This meta-analysis found—with reservations due to the above-mentioned limitations—a significant reduction in surgical bleeding and a large treatment effect of preoperative embolisation (Table 3).

The authors agreed with the strong recommendation of embolisation prior to resection surgery for symptomatic AVH [28].

It has been shown that not only embolisation, but surgical invasiveness also plays an important role in surgical bleeding in tumour surgery [7]. Due to the benign characteristics of AVH, the least invasive procedure must be applied to treat this tumour with minimal blood loss and complications. However, biomechanical considerations may compel us to perform resection and reconstruction of anterior column elements, which are associated with greater blood loss [29].

Besides this, similar to spinal tumour surgery, selective endovascular embolisation also undeniably requires skills with a learning curve [30]. The cases with greater blood loss despite embolisation indicate that it was very likely that all feeding arteries were not occluded. To improve the success rate of embolisation, a specific training program may be helpful.

There are severe methodological limitations in the meta-analysis of the published cases since significant selection and publication biases must be assumed. The inconsistency in the results reflected by the confidence interval leaves a huge question mark over the conclusion

Table 3. Summary of findings

Outcome	Illustrative comparative risks		Effect size *d*	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk without embolisation	Corresponding risk with embolisation				
Surgical blood loss (mL)	The mean surgical blood loss was 1,629 mL and ranged across control groups from 100 to 3,000 mL	The mean surgical blood loss with embolisation was 648 mL lower (p<0.05; 95% CI, 143–1,048)	0.73	51 (17)	⊕⊖⊖⊖ very low	Benefits of the significant reduction of surgical bleeding together with a strong treatment effect allow a strong recommendation for embolisation prior to AVH resection.
Embolisation for blood loss reduction in surgery for aggressive vertebral haemangioma. Patient or population: adults with aggressive vertebral haemangioma. Intervention: preoperative embolization. Comparison: surgery without embolization.						

GRADE Working Group grades of evidence.
- High quality: further research is very unlikely to change our confidence in the estimate of effect.
- Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Very low quality: we are very uncertain about the estimate.

AVH, aggressive vertebral haemangiomas.

of this study.

Further research could improve the available evidence. Pooling of prospectively collected national registry data could increase the number of included cases. Randomised controlled trials comparing embolisation to control are not feasible due to the small number of cases.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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